

Levothyroxine
EMR 200125-002

Dosage Form Proportionality of Levothyroxine New Formulations (50 µg, 100 µg, and 200 µg Tablets) in Fasted State

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Erythrocyt Period 1/ es (Day -1) (10 ¹² /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	4.767 (0.647)		4.553 (0.425)		5.120 (0.590)		4.783 (0.504)	
	Median	4.570		4.590		5.300		4.685	
	Min; Max	4.03; 5.63		4.05; 5.31		4.21; 5.86		3.85; 5.86	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	4.767 (0.669)		4.567 (0.430)		4.863 (0.665)		4.763 (0.494)	
	Median	4.655		4.590		5.120		4.805	
	Min; Max	4.00; 5.63		3.88; 5.14		3.99; 5.64		3.88; 5.64	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	4.773 (0.703)		4.475 (0.343)		5.063 (0.546)		4.768 (0.493)	
	Median	4.750		4.510		5.160		4.755	
	Min; Max	3.94; 5.62		3.86; 4.82		4.40; 5.83		3.86; 5.83	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

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Treatment C: 3 tablets of 200 µg of levothyroxine

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Erythrocyt Follow-Up es (10 ¹² /L)	n (missing) 7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	4.704 (0.276)	-0.127 (0.220)	4.674 (0.379)	-0.019 (0.257)	4.526 (0.499)	-0.119 (0.278)
	Median	4.710	-0.100	4.630	-0.110	4.470	-0.200
	Min; Max	4.26; 5.09	-0.48; 0.17	4.14; 5.24	-0.35; 0.32	3.88; 5.13	-0.55; 0.21
Hematocrit Screening (L/L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	0.403 (0.035)		0.417 (0.022)		0.416 (0.036)	
	Median	0.410		0.420		0.410	
	Min; Max	0.36; 0.44		0.39; 0.45		0.36; 0.46	
Period 1/ (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	0.406 (0.039)		0.416 (0.021)		0.409 (0.037)	
	Median	0.400		0.420		0.410	
	Min; Max	0.36; 0.46		0.39; 0.45		0.36; 0.47	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Erythrocyt Follow-Up es (10 ¹² /L)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	4.634 (0.695)	-0.050 (0.202)	4.550 (0.454)	-0.093 (0.217)	4.950 (0.628)	-0.051 (0.171)	4.673 (0.497)	-0.076 (0.216)
	Median	4.320	-0.060	4.470	-0.130	5.120	0.030	4.670	-0.085
	Min; Max	3.93; 5.57	-0.36; 0.31	3.91; 5.23	-0.40; 0.25	4.08; 5.76	-0.28; 0.17	3.88; 5.76	-0.55; 0.32
Hematocrit Screening (L/L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	0.400 (0.045)		0.409 (0.021)		0.419 (0.047)		0.410 (0.034)	
	Median	0.380		0.400		0.430		0.410	
	Min; Max	0.36; 0.47		0.39; 0.45		0.36; 0.47		0.36; 0.47	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	0.407 (0.045)		0.400 (0.022)		0.427 (0.053)		0.411 (0.037)	
	Median	0.390		0.400		0.450		0.405	
	Min; Max	0.36; 0.47		0.37; 0.44		0.36; 0.49		0.36; 0.49	

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Hematocrit Period 2/ (L/L) (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	0.410 (0.038)		0.422 (0.031)		0.413 (0.034)	
	Median	0.410		0.420		0.410	
	Min; Max	0.36; 0.47		0.38; 0.46		0.38; 0.48	
Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	0.404 (0.047)		0.420 (0.018)		0.407 (0.029)	
	Median	0.410		0.425		0.390	
	Min; Max	0.34; 0.46		0.39; 0.44		0.37; 0.44	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	0.390 (0.042)	-0.013 (0.014)	0.416 (0.022)	-0.001 (0.020)	0.406 (0.028)	-0.010 (0.026)
	Median	0.400	-0.020	0.410	0.000	0.420	-0.020
	Min; Max	0.33; 0.45	-0.03; 0.01	0.38; 0.44	-0.03; 0.02	0.37; 0.44	-0.04; 0.02

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Hematocrit Period 2/ (L/L) (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	0.407 (0.042)		0.408 (0.022)		0.403 (0.056)		0.411 (0.036)	
	Median	0.405		0.410		0.400		0.410	
	Min; Max	0.36; 0.46		0.38; 0.44		0.35; 0.47		0.35; 0.48	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	0.412 (0.044)		0.397 (0.022)		0.418 (0.052)		0.409 (0.036)	
	Median	0.415		0.395		0.410		0.410	
	Min; Max	0.36; 0.46		0.37; 0.43		0.36; 0.48		0.34; 0.48	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	0.396 (0.049)	-0.004 (0.016)	0.404 (0.032)	-0.004 (0.027)	0.409 (0.063)	-0.010 (0.020)	0.403 (0.040)	-0.007 (0.020)
	Median	0.370	-0.010	0.400	-0.010	0.430	0.000	0.410	-0.010
	Min; Max	0.35; 0.46	-0.02; 0.03	0.37; 0.44	-0.04; 0.04	0.33; 0.48	-0.05; 0.01	0.33; 0.48	-0.05; 0.04

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Hemoglobin Screening (g/L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	134.0 (15.47)		142.7 (10.64)		141.4 (15.31)	
	Median	135.0		147.0		136.0	
	Min; Max	113; 153		126; 153		118; 161	
Period 1/ (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	134.7 (17.92)		143.7 (10.06)		140.6 (17.33)	
	Median	132.0		146.0		138.0	
	Min; Max	107; 157		133; 158		117; 165	
Period 2/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	135.1 (17.64)		145.7 (13.94)		140.4 (15.23)	
	Median	136.0		150.0		137.0	
	Min; Max	111; 159		128; 158		122; 168	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Hemoglobin Screening (g/L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	135.4 (17.55)		140.6 (10.34)		138.9 (20.84)		138.8 (14.85)	
	Median	130.0		139.0		149.0		137.5	
	Min; Max	116; 162		129; 161		109; 162		109; 162	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	137.7 (17.42)		137.4 (11.75)		142.3 (22.79)		139.4 (16.00)	
	Median	133.0		136.0		152.0		137.5	
	Min; Max	115; 163		124; 158		114; 169		107; 169	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	139.8 (16.22)		138.2 (12.92)		134.0 (24.56)		138.8 (16.39)	
	Median	139.0		136.0		132.0		138.5	
	Min; Max	118; 161		122; 159		110; 164		110; 168	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Hemoglobin Period 3/ (g/L) (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	134.4 (19.84)		144.5 (9.65)		138.0 (13.67)	
	Median	140.0		148.5		134.0	
	Min; Max	104; 156		131; 155		119; 154	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	127.9 (18.22)	-6.1 (6.28)	141.9 (11.52)	-0.9 (7.78)	136.0 (13.81)	-5.4 (8.54)
	Median	133.0	-7.0	140.0	-2.0	139.0	-5.0
	Min; Max	100; 153	-13; 3	127; 159	-11; 9	115; 155	-17; 6
Leukocytes Screening (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)	
	Mean (SD)	5.203 (0.917)		5.163 (0.716)		5.541 (1.205)	
	Median	5.190		5.150		5.460	
	Min; Max	3.76; 6.79		4.47; 6.45		4.01; 7.59	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Hemoglobin Period 3/ (g/L) (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	139.2 (16.93)		136.0 (10.32)		137.2 (23.71)		138.1 (15.69)	
	Median	139.0		132.5		135.5		137.0	
	Min; Max	119; 160		123; 149		114; 167		104; 167	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	133.6 (18.27)	-1.9 (3.80)	137.0 (14.92)	-3.6 (8.98)	135.3 (26.19)	-3.6 (8.22)	135.3 (17.19)	-3.6 (7.25)
	Median	126.0	-3.0	128.0	-6.0	151.0	0.0	135.5	-3.0
	Min; Max	114; 161	-6; 6	123; 158	-16; 10	106; 164	-20; 3	100; 164	-20; 10
Leukocytes Screening (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	5.784 (1.322)		5.287 (1.245)		5.069 (1.185)		5.341 (1.078)	
	Median	5.730		5.100		5.310		5.300	
	Min; Max	3.75; 7.24		3.66; 7.23		3.53; 6.49		3.53; 7.59	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Leukocytes Period 1/ (10 ⁹ /L) (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	5.379 (0.888)		5.313 (0.589)		6.321 (2.423)	
	Median	4.950		5.160		5.470	
	Min; Max	4.39; 7.07		4.73; 6.44		4.80; 11.60	
Period 2/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	5.719 (0.788)		5.318 (1.015)		5.180 (1.098)	
	Median	5.850		5.280		4.910	
	Min; Max	4.08; 6.40		3.62; 6.52		3.92; 7.10	
Period 3/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	6.300 (1.292)		5.147 (1.134)		4.990 (0.857)	
	Median	6.160		4.880		4.800	
	Min; Max	4.59; 8.59		3.83; 7.26		3.91; 6.48	

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Leukocytes Period 1/ (10 ⁹ /L) (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	6.257 (1.560)		5.657 (1.238)		5.211 (1.261)		5.690 (1.429)	
	Median	5.970		5.580		5.690		5.505	
	Min; Max	3.48; 7.91		3.97; 7.49		3.41; 6.97		3.41; 11.60	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	6.078 (1.734)		6.245 (1.972)		4.575 (0.799)		5.516 (1.330)	
	Median	5.455		5.670		4.525		5.415	
	Min; Max	4.39; 9.35		4.42; 9.92		3.73; 5.49		3.62; 9.92	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	5.595 (1.019)		6.778 (2.777)		5.173 (0.811)		5.663 (1.511)	
	Median	5.820		6.625		4.935		5.285	
	Min; Max	3.75; 6.47		3.55; 10.32		4.49; 6.61		3.55; 10.32	

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Leukocytes Follow-Up (10 ⁹ /L)	n (missing) 7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	5.389 (1.036)	0.186 (1.180)	5.734 (1.941)	0.571 (1.385)	5.529 (0.889)	-0.013 (0.914)
	Median	5.020	-0.050	4.810	0.220	5.550	-0.210
	Min; Max	4.46; 7.51	-0.91; 2.59	4.58; 9.99	-0.61; 3.54	3.84; 6.37	-1.22; 1.54
Lymphocyte Screenings (10 ⁹ /L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	1.471 (0.278)		1.621 (0.329)		1.689 (0.406)	
	Median	1.470		1.650		1.440	
	Min; Max	0.98; 1.82		1.18; 2.12		1.22; 2.20	
Period 1/ (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	1.731 (0.266)		1.674 (0.478)		1.746 (0.432)	
	Median	1.650		1.660		1.820	
	Min; Max	1.48; 2.24		1.04; 2.43		0.95; 2.26	

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 Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Leukocytes Follow-Up (10 ⁹ /L)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	5.711 (1.088)	-0.073 (1.233)	5.703 (1.492)	0.416 (0.736)	4.987 (1.058)	-0.081 (0.733)	5.509 (1.248)	0.168 (1.025)
	Median	6.130	-0.440	5.300	0.200	4.680	-0.050	5.335	0.015
	Min; Max	3.94; 6.89	-1.58; 1.734	2.0; 8.67	-0.50; 1.443	0.65; 6.28	-0.91; 0.783	0.65; 9.99	-1.58; 3.54
Lymphocyte Screenings (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	1.710 (0.382)		1.661 (0.314)		1.410 (0.199)		1.594 (0.325)	
	Median	1.720		1.550		1.320		1.500	
	Min; Max	1.09; 2.20		1.38; 2.29		1.26; 1.79		0.98; 2.29	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	2.087 (0.509)		1.979 (0.638)		1.709 (0.451)		1.821 (0.472)	
	Median	2.140		1.570		1.640		1.760	
	Min; Max	1.34; 2.75		1.42; 2.88		1.15; 2.43		0.95; 2.88	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Lymphocyte Period 2/ s (10 ⁹ /L) (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	1.843 (0.392)		1.837 (0.466)		1.731 (0.558)	
	Median	1.790		1.960		1.510	
	Min; Max	1.43; 2.57		1.18; 2.29		1.09; 2.49	
Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	1.720 (0.477)		1.500 (0.344)		1.643 (0.339)	
	Median	1.850		1.510		1.630	
	Min; Max	1.03; 2.44		1.00; 1.92		1.13; 2.19	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	1.551 (0.187)	0.080 (0.300)	1.716 (0.333)	0.094 (0.326)	1.604 (0.354)	-0.084 (0.227)
	Median	1.570	-0.050	1.740	0.110	1.530	-0.130
	Min; Max	1.29; 1.87	-0.24; 0.59	1.29; 2.23	-0.37; 0.58	1.04; 2.05	-0.45; 0.27

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Lymphocyte Period 2/ s (10 ⁹ /L) (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	2.047 (0.443)		2.082 (0.491)		1.500 (0.284)		1.837 (0.461)	
	Median	2.080		1.935		1.390		1.815	
	Min; Max	1.33; 2.65		1.54; 2.71		1.17; 1.92		1.09; 2.71	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	1.687 (0.413)		1.675 (0.211)		1.487 (0.236)		1.622 (0.342)	
	Median	1.880		1.670		1.485		1.640	
	Min; Max	0.94; 2.04		1.43; 1.97		1.23; 1.78		0.94; 2.44	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	1.844 (0.537)	0.134 (0.322)	1.713 (0.374)	0.051 (0.222)	1.467 (0.267)	0.057 (0.204)	1.649 (0.358)	0.055 (0.264)
	Median	1.890	0.110	1.540	0.020	1.460	0.180	1.575	0.030
	Min; Max	1.04; 2.83	-0.22; 0.79	1.41; 2.34	-0.17; 0.51	1.12; 1.82	-0.22; 0.25	1.04; 2.83	-0.45; 0.79

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Lymphocyte Screening s/Leukocytes (%)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	29.23 (8.067)		31.34 (4.509)		31.26 (7.738)	
	Median	28.90		29.90		34.00	
	Min; Max	17.6; 39.1		26.4; 40.6		18.8; 38.8	
Period 1/ (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	32.59 (5.324)		31.61 (8.571)		30.06 (11.378)	
	Median	31.70		31.80		34.70	
	Min; Max	26.8; 41.0		18.5; 45.5		16.6; 43.3	
Period 2/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	32.74 (8.057)		34.43 (5.367)		33.86 (9.945)	
	Median	31.50		33.25		35.50	
	Min; Max	24.4; 45.1		28.2; 44.2		21.3; 48.1	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Lymphocyte Screening s/Leukocytes (%)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	30.29 (6.672)		31.67 (10.172)		28.96 (6.619)		30.46 (7.104)	
	Median	30.40		30.90		29.30		30.15	
	Min; Max	21.1; 38.6		14.1; 45.8		19.4; 39.1		14.1; 45.8	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	34.04 (6.564)		35.44 (9.081)		32.97 (4.663)		32.79 (7.641)	
	Median	37.80		39.40		34.90		34.00	
	Min; Max	25.4; 40.5		19.0; 46.0		25.5; 37.3		16.6; 46.0	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	34.37 (6.061)		35.15 (10.023)		33.02 (4.473)		33.89 (7.240)	
	Median	33.85		37.05		33.60		33.50	
	Min; Max	28.3; 42.0		19.7; 46.0		25.7; 38.2		19.7; 48.1	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Lymphocyte Period 3/ s/Leukocyt (Day -1) es (%)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	28.47 (10.167)		29.62 (6.312)		33.60 (8.545)	
	Median	25.00		30.80		32.40	
	Min; Max	14.4; 42.5		19.3; 36.9		23.5; 47.4	
Follow-Up	n (missing) 7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	29.93 (7.839)	0.70 (6.908)	31.13 (5.958)	-0.21 (5.539)	30.00 (9.346)	-1.26 (8.103)
	Median	31.30	-1.10	31.40	0.20	28.20	-1.30
	Min; Max	19.0; 41.9	-9.3; 13.7	20.4; 38.0	-9.5; 8.4	16.8; 43.5	-10.9; 11.9
Monocytes Screening (10 ⁹ /L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	0.550 (0.165)		0.484 (0.106)		0.526 (0.140)	
	Median	0.520		0.430		0.460	
	Min; Max	0.38; 0.80		0.34; 0.60		0.35; 0.78	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Lymphocyte Period 3/ s/Leukocyt (Day -1) es (%)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	30.13 (5.647)		29.02 (13.159)		28.92 (3.797)		30.02 (8.180)	
	Median	30.15		27.55		28.95		30.10	
	Min; Max	22.7; 37.2		15.5; 45.3		24.5; 34.2		14.4; 47.4	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	32.30 (7.052)	2.01 (5.404)	32.11 (12.154)	0.44 (5.988)	29.73 (3.336)	0.77 (6.209)	30.87 (7.656)	0.41 (6.104)
	Median	30.70	4.50	32.30	1.40	29.90	1.40	30.70	1.20
	Min; Max	24.2; 41.5	-7.9; 7.8	16.3; 55.7	-8.5; 9.9	25.1; 35.7	-11.4; 8.3	16.3; 55.7	-11.4; 13.7
Monocytes (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	0.546 (0.172)		0.517 (0.137)		0.493 (0.133)		0.519 (0.137)	
	Median	0.530		0.540		0.500		0.510	
	Min; Max	0.39; 0.89		0.34; 0.72		0.30; 0.64		0.30; 0.89	

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 Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)		
		Observed	Change	Observed	Change	Observed	Change	
Monocytes (10 ⁹ /L)	Period 1/ (Day -1)	n (missing)	7 (0)			7 (0)		
	Mean (SD)	0.597 (0.183)		0.559 (0.215)		0.619 (0.242)		
	Median	0.550		0.470		0.540		
	Min; Max	0.45; 0.96		0.38; 0.91		0.36; 1.04		
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	0.587 (0.118)		0.498 (0.125)		0.519 (0.179)		
	Median	0.590		0.465		0.560		
	Min; Max	0.44; 0.78		0.33; 0.65		0.19; 0.76		
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
Mean (SD)	0.697 (0.343)		0.525 (0.183)		0.476 (0.120)			
Median	0.590		0.500		0.540			
Min; Max	0.46; 1.44		0.33; 0.77		0.30; 0.58			

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;
 Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine
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Dosage Form Proportionality of Levothyroxine New Formulations (50 µg, 100 µg, and 200 µg Tablets) in Fasted State

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 Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Monocytes (10 ⁹ /L)	Period 1/ (Day -1)	n (missing) 7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	0.594 (0.166)		0.571 (0.170)		0.526 (0.121)		0.578 (0.178)	
	Median	0.560		0.610		0.500		0.540	
	Min; Max	0.33; 0.84		0.36; 0.80		0.36; 0.70		0.33; 1.04	
	Period 2/ (Day -1)	n (missing) 6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	0.587 (0.103)		0.642 (0.199)		0.438 (0.069)		0.546 (0.147)	
	Median	0.585		0.610		0.440		0.540	
	Min; Max	0.45; 0.75		0.44; 0.93		0.34; 0.53		0.19; 0.93	
	Period 3/ (Day -1)	n (missing) 6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	0.587 (0.123)		0.678 (0.192)		0.503 (0.063)		0.578 (0.203)	
	Median	0.620		0.670		0.500		0.560	
	Min; Max	0.39; 0.75		0.36; 0.89		0.44; 0.57		0.30; 1.44	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Monocytes Follow-Up (10 ⁹ /L)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	0.523 (0.105)	-0.027 (0.132)	0.609 (0.282)	0.124 (0.245)	0.533 (0.214)	0.007 (0.095)
	Median	0.500	-0.010	0.510	0.030	0.430	-0.020
	Min; Max	0.42; 0.75	-0.29; 0.11	0.43; 1.23	-0.09; 0.65	0.36; 0.96	-0.09; 0.18
Monocytes/ Screening Leukocytes (%)	n (missing)	7 (0)		7 (0)		7 (0)	
	Mean (SD)	10.49 (2.056)		9.46 (1.890)		9.59 (2.224)	
	Median	10.50		9.40		8.70	
	Min; Max	8.3; 14.4		6.0; 11.7		7.9; 14.3	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
	Mean (SD)	10.96 (1.652)		10.36 (3.247)		9.93 (2.507)	
	Median	10.70		8.80		10.60	
	Min; Max	9.2; 13.6		7.8; 15.9		6.6; 13.9	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Monocytes Follow-Up (10 ⁹ /L)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	0.630 (0.159)	0.084 (0.151)	0.544 (0.142)	0.027 (0.107)	0.470 (0.125)	-0.023 (0.101)	0.551 (0.178)	0.032 (0.149)
	Median	0.580	0.030	0.570	0.010	0.440	0.010	0.510	0.010
	Min; Max	0.46; 0.89	-0.08; 0.38	0.35; 0.73	-0.16; 0.17	0.32; 0.63	-0.17; 0.13	0.32; 1.23	-0.29; 0.65
Monocytes/ Screening Leukocytes (%)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	9.47 (1.898)		9.49 (2.506)		9.73 (1.430)		9.70 (1.935)	
	Median	8.70		9.60		10.10		9.40	
	Min; Max	7.5; 12.3		5.6; 12.3		7.7; 11.5		5.6; 14.4	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	9.60 (1.848)		10.27 (3.120)		10.23 (1.433)		10.22 (2.294)	
	Median	9.50		9.30		10.60		9.90	
	Min; Max	7.3; 12.7		6.8; 15.4		7.2; 11.4		6.6; 15.9	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

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 Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Monocytes/ Period 2/ Leukocytes (Day -1) (%)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	10.31 (1.872)		9.30 (0.817)		9.89 (2.736)	
	Median	9.70		9.30		10.70	
	Min; Max	8.0; 14.0		8.2; 10.5		4.8; 12.5	
Period 3/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	10.93 (4.180)		10.13 (2.724)		9.51 (1.868)	
	Median	10.00		9.30		9.70	
	Min; Max	7.5; 20.1		7.2; 14.9		6.5; 11.7	
Follow-Up	n (missing) 7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	9.86 (1.906)	-0.63 (1.872)	10.47 (1.968)	1.01 (1.781)	9.59 (3.100)	0.00 (1.303)
	Median	10.20	-0.30	10.40	1.00	8.00	0.10
	Min; Max	6.9; 12.8	-4.2; 1.9	8.2; 13.7	-1.1; 3.3	6.5; 15.5	-2.2; 1.5

Baseline defined as Screening for Follow-Up results.

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Monocytes/ Period 2/ Leukocytes (Day -1) (%)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	10.10 (2.672)		10.73 (3.676)		9.65 (1.067)		10.00 (2.242)	
	Median	9.55		10.35		9.45		9.60	
	Min; Max	6.7; 13.7		6.8; 16.7		8.3; 11.4		4.8; 16.7	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	10.48 (0.983)		10.63 (2.752)		9.80 (0.965)		10.25 (2.437)	
	Median	10.30		9.70		9.90		9.90	
	Min; Max	9.3; 11.7		7.8; 14.7		8.3; 11.2		6.5; 20.1	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	11.29 (3.064)	1.81 (2.036)	9.83 (2.724)	0.34 (1.189)	9.37 (1.147)	-0.36 (1.772)	10.07 (2.362)	0.36 (1.791)
	Median	10.10	2.40	10.90	0.50	9.60	-0.90	10.15	0.15
	Min; Max	7.7; 15.7	-1.1; 3.8	6.7; 13.6	-2.1; 1.3	7.6; 10.8	-2.0; 3.1	6.5; 15.7	-4.2; 3.8

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Neutrophil Screenings (10 ⁹ /L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	2.989 (0.783)		2.846 (0.610)		3.117 (1.114)	
	Median	2.920		2.740		2.800	
	Min; Max	1.79; 4.16		2.19; 3.77		1.98; 5.42	
Period 1/ (Day -1)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	2.847 (0.520)		2.831 (0.395)		3.777 (2.272)	
	Median	2.880		2.810		2.750	
	Min; Max	2.04; 3.49		2.26; 3.42		2.12; 8.57	
Period 2/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	3.067 (0.708)		2.707 (0.573)		2.731 (0.950)	
	Median	3.230		2.800		2.630	
	Min; Max	1.71; 3.86		1.99; 3.46		1.85; 4.69	

Baseline defined as Screening for Follow-Up results.

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Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Neutrophil Screening s (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	3.323 (1.132)		3.003 (1.246)		2.996 (1.057)		3.045 (0.962)	
	Median	3.180		3.040		3.010		2.935	
	Min; Max	1.98; 4.89		1.56; 5.25		1.76; 4.62		1.56; 5.42	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	3.359 (1.157)		2.869 (1.043)		2.773 (0.836)		3.076 (1.190)	
	Median	3.620		2.570		2.860		2.820	
	Min; Max	1.69; 5.12		1.88; 5.03		1.72; 3.96		1.69; 8.57	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	3.172 (1.439)		3.248 (1.764)		2.467 (0.614)		2.899 (1.050)	
	Median	2.430		2.715		2.350		2.635	
	Min; Max	2.11; 5.83		1.81; 6.74		1.89; 3.43		1.71; 6.74	

Baseline defined as Screening for Follow-Up results.

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Neutrophil Period 3/ s (10 ⁹ /L) (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	3.741 (1.216)		2.898 (0.860)		2.686 (0.825)	
	Median	3.610		2.605		2.730	
	Min; Max	2.09; 5.67		2.13; 4.47		1.84; 4.11	
Follow-Up	n (missing) 7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	3.127 (1.120)	0.139 (1.109)	3.167 (1.483)	0.321 (1.092)	3.160 (0.914)	0.043 (0.974)
	Median	2.720	0.020	2.710	-0.050	3.400	-0.190
	Min; Max	2.01; 5.40	-0.90; 2.48	1.98; 6.46	-0.62; 2.69	1.60; 4.14	-1.28; 1.46
Neutrophil Screening s/Leukocytes (%)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	56.76 (6.706)		54.96 (7.449)		55.29 (8.250)	
	Median	59.30		56.60		53.00	
	Min; Max	47.6; 65.1		41.9; 63.0		46.4; 71.4	

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Neutrophil Period 3/ s (10 ⁹ /L) (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		36 (0)	
	Mean (SD)	3.053 (0.794)		4.078 (2.652)		2.977 (0.539)		3.238 (1.334)	
	Median	2.995		3.935		2.845		2.905	
	Min; Max	2.26; 4.12		1.20; 7.15		2.51; 3.98		1.20; 7.15	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	2.911 (0.888)	-0.411 (0.724)	3.187 (1.634)	0.184 (0.666)	2.881 (0.748)	-0.114 (0.712)	3.072 (1.110)	0.027 (0.876)
	Median	2.520	-0.530	3.020	0.110	2.690	0.080	2.725	-0.015
	Min; Max	1.97; 4.36	-1.37; 0.51	1.05; 6.35	-0.52; 1.10	1.96; 3.84	-1.09; 0.87	1.05; 6.46	-1.37; 2.69
Neutrophil Screening s/Leukocytes (%)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	56.51 (9.041)		55.59 (12.718)		57.70 (7.962)		56.13 (8.396)	
	Median	55.50		57.70		57.10		56.60	
	Min; Max	44.4; 69.3		38.9; 77.2		47.3; 71.2		38.9; 77.2	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Neutrophil Period 1/ s/Leukocyt (Day -1) es (%)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	52.96 (5.467)		53.44 (6.208)		56.73 (11.760)	
	Median	52.00		53.30		52.40	
	Min; Max	46.5; 59.7		42.3; 60.6		44.2; 73.8	
Period 2/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	53.09 (7.345)		50.98 (5.344)		52.16 (9.530)	
	Median	53.30		52.55		53.00	
	Min; Max	41.9; 61.8		40.9; 55.3		37.7; 66.0	
Period 3/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	58.31 (9.413)		55.82 (5.665)		53.01 (8.679)	
	Median	61.20		54.90		52.30	
	Min; Max	45.6; 69.9		47.9; 62.9		39.8; 63.3	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics n (missing)	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Neutrophil Period 1/ s/Leukocytes (%)	7 (0)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	52.89 (8.133)		50.20 (9.822)		52.70 (5.069)		53.15 (7.845)	
	Median	49.80		47.40		52.10		52.05	
	Min; Max	43.8; 64.7		36.5; 67.1		44.4; 59.2		36.5; 73.8	
Period 2/ (Day -1)	6 (0)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	50.83 (9.392)		49.90 (9.783)		53.47 (5.160)		51.78 (7.578)	
	Median	50.35		47.20		52.65		52.30	
	Min; Max	38.7; 62.5		41.0; 67.9		47.3; 62.4		37.7; 67.9	
Period 3/ (Day -1)	6 (0)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	54.45 (8.237)		54.40 (17.649)		57.45 (2.722)		55.58 (9.319)	
	Median	56.75		57.50		57.40		56.20	
	Min; Max	41.9; 63.7		33.9; 73.3		54.5; 60.5		33.9; 73.3	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Neutrophil Follow-Up s/Leukocytes (%)	n (missing) 7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	56.70 (8.741)	-0.06 (6.977)	53.97 (7.086)	-0.99 (6.265)	56.21 (9.920)	0.93 (9.449)
	Median	54.40	0.80	54.90	0.90	62.00	-0.20
	Min; Max	45.1; 71.9	-11.0; 12.6	42.8; 64.7	-13.5; 6.2	41.7; 65.8	-14.4; 12.5
Platelets (10 ⁹ /L)	Screening n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	288.7 (57.86)		257.1 (95.14)		252.1 (48.66)	
	Median	258.0		239.0		251.0	
	Min; Max	223; 368		158; 437		170; 327	
	Period 1/ (Day -1) n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	300.3 (61.64)		249.3 (76.80)		267.9 (58.89)	
	Median	286.0		236.0		266.0	
	Min; Max	217; 401		178; 378		167; 353	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Neutrophil Follow-Up s/Leukocytes (%)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	50.84 (10.475)	-5.67 (3.727)	53.29 (14.981)	-2.30 (6.275)	57.40 (5.377)	-0.30 (7.177)	54.74 (9.558)	-1.40 (6.782)
	Median	44.50	-4.10	56.90	-3.60	57.50	-0.70	55.95	-1.20
	Min; Max	40.3; 65.7	-12.1; -1.2	25.0; 73.2	-13.9; 4.7	46.6; 62.8	-10.5; 13.0	25.0; 73.2	-14.4; 13.0
Platelets (10 ⁹ /L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	240.9 (52.14)		278.3 (51.18)		249.3 (68.98)		261.1 (62.68)	
	Median	228.0		268.0		257.0		248.5	
	Min; Max	196; 352		229; 383		165; 359		158; 437	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	248.6 (56.00)		291.1 (41.72)		259.1 (54.28)		269.4 (58.96)	
	Median	232.0		287.0		263.0		265.0	
	Min; Max	180; 350		242; 373		177; 339		167; 401	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine
Treatment C: 3 tablets of 200 µg of levothyroxine/project24/ep/blinded/e210898_merc/stats/versioncontrol/primary/scripts/program/main/TFL programs/Tables/Table
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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Platelets (10 ⁹ /L)	Period 2/ (Day -1)	n (missing) 7 (0)		6 (0)		7 (0)	
	Mean (SD)	295.1 (56.76)		271.5 (94.35)		263.0 (61.47)	
	Median	287.0		248.0		261.0	
	Min; Max	226; 399		171; 428		166; 361	
Period 3/ (Day -1)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	287.3 (70.68)		262.3 (109.75)		257.4 (40.70)	
	Median	284.0		224.5		270.0	
	Min; Max	191; 401		156; 446		175; 300	
Follow-Up	n (missing) 7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	290.4 (51.24)	1.7 (43.89)	258.9 (79.43)	1.7 (27.07)	267.9 (50.55)	15.7 (22.19)
	Median	284.0	19.0	249.0	0.0	267.0	14.0
	Min; Max	212; 382	-88; 36	157; 397	-40; 46	184; 329	-20; 44

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.1 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Hematology (Safety Population)

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Platelets Period 2/ (10 ⁹ /L) (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	242.8 (46.64)		321.7 (65.44)		274.2 (64.74)		278.1 (66.29)	
	Median	236.5		295.5		252.0		266.5	
	Min; Max	188; 308		266; 442		192; 369		166; 442	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	258.0 (47.39)		288.8 (39.27)		290.7 (65.12)		274.0 (63.41)	
	Median	267.0		286.0		304.5		271.0	
	Min; Max	188; 313		250; 357		191; 358		156; 446	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	252.9 (41.61)	12.0 (24.59)	296.0 (56.75)	17.7 (32.42)	256.7 (65.86)	7.4 (38.89)	270.5 (57.70)	9.4 (31.07)
	Median	261.0	15.0	289.0	12.0	261.0	15.0	265.0	13.0
	Min; Max	200; 318	-34; 42	247; 375	-16; 84	164; 349	-67; 54	157; 397	-88; 84

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA;

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Alanine Aminotransferase (U/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	17.67 (14.317)		17.06 (9.878)		17.91 (7.595)	
		Median	12.70		12.50		19.20	
		Min; Max	8.5; 48.8		3.1; 31.4		6.2; 28.5	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	16.40 (15.601)		14.80 (9.649)		16.46 (8.673)	
		Median	12.30		12.80		14.40	
		Min; Max	3.7; 50.9		3.8; 34.7		8.4; 32.0	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	18.23 (11.183)		19.78 (7.207)		20.86 (14.055)	
		Median	13.90		19.05		15.20	
		Min; Max	9.2; 41.1		12.0; 31.7		10.3; 50.1	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit)	Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Alanine Aminotransf erase (U/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	19.73 (12.219)		17.70 (8.372)		16.64 (7.235)		17.79 (9.667)	
		Median	14.10		21.30		14.40		14.90	
		Min; Max	7.7; 40.0		5.2; 27.3		5.1; 28.5		3.1; 48.8	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	17.60 (9.915)		19.21 (11.937)		16.23 (4.853)		16.78 (10.041)	
		Median	15.10		14.90		16.60		13.75	
		Min; Max	6.9; 34.1		6.7; 42.4		8.1; 22.3		3.7; 50.9	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	19.62 (11.131)		16.63 (7.971)		21.28 (11.573)		19.41 (10.260)	
		Median	15.30		16.35		18.90		15.45	
		Min; Max	10.5; 40.8		7.5; 28.3		12.0; 43.4		7.5; 50.1	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Alanine Aminotransferase (U/L)	Period 3/ n (missing)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	20.93 (17.417)		19.37 (6.668)		17.77 (6.470)	
		Median	15.30		17.40		19.70	
	Min; Max	7.8; 59.2		13.5; 30.6		10.0; 25.5		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
Mean (SD)		23.59 (18.566)	5.91 (13.095)	18.31 (8.343)	1.26 (10.379)	18.73 (7.464)	0.81 (5.432)	
Median		15.10	2.30	18.70	2.80	15.40	3.10	
Min; Max	9.5; 53.1	-5.7; 34.4	4.5; 29.5	-17.5; 14.0	11.6; 31.9	-10.2; 5.4		
Alkaline Phosphatase (U/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	59.87 (14.261)		61.24 (5.764)		75.00 (19.782)	
	Median	64.40		59.40		76.40		
	Min; Max	38.7; 77.5		55.0; 70.6		47.2; 96.4		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Alanine Aminotransf (Day -1) erase (U/L)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	26.37 (18.699)		16.48 (6.754)		15.93 (3.810)		19.47 (11.380)	
	Median	19.65		15.50		16.25		16.25	
	Min; Max	11.8; 60.4		9.4; 26.9		11.7; 22.1		7.8; 60.4	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	26.76 (14.091)	7.03 (15.201)	17.36 (7.585)	-0.34 (3.790)	14.00 (2.976)	-2.64 (6.913)	19.79 (11.207)	2.00 (9.999)
	Median	30.60	5.80	15.20	0.40	15.00	-0.20	15.40	1.65
	Min; Max	8.3; 49.2	-5.8; 37.8	9.1; 27.7	-6.1; 3.9	8.9; 17.0	-17.3; 3.8	4.5; 53.1	-17.5; 37.8
Alkaline Phosphatase (U/L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	76.71 (18.586)		65.30 (19.818)		71.69 (19.757)		68.30 (17.347)	
	Median	72.70		69.60		71.40		68.25	
	Min; Max	59.0; 117.1		39.0; 89.9		43.2; 103.2		38.7; 117.1	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Alkaline Phosphatase (Day -1) (U/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	61.40 (12.068)		59.66 (5.722)		75.11 (17.162)	
		Median	67.10		60.60		82.10	
		Min; Max	38.6; 69.8		53.5; 70.7		49.1; 95.8	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	57.94 (13.021)		58.73 (5.557)		69.39 (17.508)	
		Median	64.10		58.30		74.10	
		Min; Max	35.5; 70.9		51.8; 66.5		40.1; 83.4	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	58.24 (13.879)		56.53 (7.707)		66.89 (16.634)	
		Median	66.60		53.05		69.30	
		Min; Max	32.6; 70.8		51.5; 71.5		41.2; 90.4	

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Alkaline Phosphatase (Day -1) (U/L)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	80.01 (17.889)		65.00 (16.238)		74.14 (19.474)		69.22 (16.407)	
	Median	73.40		68.10		69.50		69.05	
	Min; Max	59.7; 114.2		43.3; 87.0		43.2; 104.3		38.6; 114.2	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	75.37 (13.539)		66.27 (19.224)		67.75 (16.517)		65.79 (15.187)	
	Median	72.55		67.00		68.30		65.35	
	Min; Max	60.0; 100.8		41.9; 88.2		42.9; 90.6		35.5; 100.8	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	78.43 (21.280)		61.80 (17.130)		71.35 (16.243)		65.38 (16.700)	
	Median	75.10		59.65		72.40		67.05	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	56.6; 118.5		37.4; 82.4		47.2; 94.3		32.6; 118.5	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Alkaline Phosphatase (U/L)	Follow-Up	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	54.90 (11.997)	-4.97 (10.919)	56.63 (6.526)	-4.61 (3.554)	65.84 (15.120)	-9.16 (6.731)
		Median	57.50	-3.30	56.50	-3.40	70.70	-10.70
		Min; Max	34.7; 67.9	-27.0; 4.5	47.1; 69.0	-9.1; -0.9	45.0; 82.9	-20.2; -2.2
Amylase (IU/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	62.14 (16.328)		57.61 (15.535)		60.79 (18.349)	
		Median	66.00		57.00		61.10	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	60.16 (18.992)		55.77 (7.562)		52.67 (15.844)	
		Median	60.20		51.60		54.10	
		Min; Max	34.3; 86.9		48.1; 65.7		33.0; 76.5	

Baseline defined as Screening for Follow-Up results.

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Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics n (missing)	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Alkaline Phosphatase (U/L)	Follow-Up		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	77.39 (15.618)	0.67 (6.832)	62.31 (18.946)	-2.99 (5.302)	71.33 (17.422)	-0.36 (6.928)	64.73 (16.034)	-3.57 (7.392)
		Median	77.60	0.50	71.20	-2.80	69.20	0.50	66.40	-3.05
		Min; Max	59.5; 109.0	-8.1; 8.7	38.1; 80.0	-9.9; 5.0	43.7; 96.0	-7.2; 11.2	34.7; 109.0	-27.0; 11.2
Amylase (IU/L)	Screening		7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	61.56 (16.922)		55.97 (25.382)		52.93 (15.530)		58.50 (17.503)	
		Median	64.90		69.00		52.50		57.80	
		Min; Max	32.7; 82.8		19.3; 85.1		31.9; 79.2		19.3; 88.5	
	Period 1/ (Day -1)		7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	63.36 (17.315)		56.11 (23.026)		50.80 (11.631)		56.48 (16.051)	
		Median	64.80		66.40		53.90		55.65	
		Min; Max	37.2; 91.0		22.1; 84.1		31.0; 64.3		22.1; 91.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)		
			Observed	Change	Observed	Change	Observed	Change	
Amylase (IU/L)	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)		
		Mean (SD)	67.14 (21.891)		59.87 (13.050)		57.06 (17.620)		
		Median	68.00		54.85		57.20		
		Min; Max	36.4; 93.5		47.3; 78.0		33.7; 78.3		
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)		
		Mean (SD)	65.13 (23.164)		58.53 (12.733)		57.39 (16.215)		
		Median	68.50		60.80		55.20		
		Min; Max	36.0; 92.6		41.4; 73.2		37.2; 84.9		
	Follow-Up	n (missing)	7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	
		Mean (SD)	67.43 (23.205)		5.29 (14.130)	57.36 (5.597)	-0.26 (16.264)	59.37 (16.606)	-1.41 (8.123)
		Median	62.00		2.70	57.10	1.00	64.50	-0.50
		Min; Max	39.8; 101.5		-6.4; 33.4	48.3; 66.4	-33.3; 17.2	34.7; 78.6	-17.4; 9.9

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Amylase (IU/L)	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	67.57 (22.551)		54.18 (27.621)		51.87 (16.771)		59.74 (19.941)	
		Median	69.75		53.70		52.25		62.10	
		Min; Max	35.0; 97.3		17.8; 89.3		32.1; 70.3		17.8; 97.3	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	64.67 (18.926)		48.02 (19.519)		57.12 (18.600)		58.62 (18.194)	
		Median	63.10		50.15		57.85		60.40	
		Min; Max	40.3; 97.3		23.1; 66.8		32.4; 83.6		23.1; 97.3	
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	63.74 (16.856)	2.19 (6.298)	55.00 (24.321)	-0.97 (10.918)	51.69 (13.336)	-1.24 (6.701)	59.10 (17.499)	0.60 (10.649)
		Median	63.60	1.50	61.10	-1.10	50.10	-1.80	59.25	-0.05
		Min; Max	41.0; 94.7	-7.3; 11.9	22.3; 87.6	-13.9; 18.6	30.1; 68.0	-11.2; 9.2	22.3; 101.5	-33.3; 33.4

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Aspartate Aminotransferase (U/L)	Screening n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	20.03 (4.740)		23.41 (5.695)		21.91 (5.307)	
	Median	18.60		24.20		23.60	
	Min; Max	15.7; 29.4		16.8; 33.0		15.8; 30.4	
	Period 1/ (Day -1)	n (missing) 7 (0)		7 (0)		7 (0)	
	Mean (SD)	19.93 (4.694)		19.21 (3.318)		22.87 (7.114)	
	Median	18.80		20.30		22.50	
	Min; Max	14.8; 29.6		15.0; 23.7		15.0; 33.9	
	Period 2/ (Day -1)	n (missing) 7 (0)		6 (0)		7 (0)	
	Mean (SD)	18.97 (5.219)		19.12 (3.805)		33.97 (36.616)	
	Median	17.80		18.80		20.90	
	Min; Max	13.0; 27.0		14.7; 25.1		15.0; 116.3	

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Aspartate Aminotransferase (U/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	23.00 (3.460)		22.36 (4.480)		21.20 (4.065)		21.99 (4.536)	
		Median	21.80		22.50		21.90		22.00	
		Min; Max	19.4; 28.2		16.1; 29.9		14.3; 25.9		14.3; 33.0	
Period 1/ (Day -1)		n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	22.69 (3.336)		22.71 (5.617)		22.60 (6.796)		21.67 (5.249)	
		Median	22.70		20.30		20.30		20.50	
		Min; Max	18.2; 29.1		17.0; 33.7		14.7; 36.1		14.7; 36.1	
Period 2/ (Day -1)		n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	21.65 (4.679)		20.73 (3.278)		23.48 (9.953)		23.17 (16.462)	
		Median	20.20		20.75		22.00		20.65	
		Min; Max	17.4; 29.4		15.6; 25.4		13.2; 38.1		13.0; 116.3	

Baseline defined as Screening for Follow-Up results.

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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Aspartate Period 3/ Aminotransf (Day -1) erase (U/L)	n (missing) 7 (0)			6 (0)		7 (0)	
	Mean (SD)	19.73 (4.863)		20.43 (3.877)		22.01 (7.387)	
	Median	17.80		20.05		19.40	
	Min; Max	16.6; 30.3		16.3; 26.8		13.6; 31.5	
Follow-Up	n (missing) 7 (0)		7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
	Mean (SD)	20.49 (7.452)	0.46 (6.770)	20.46 (5.777)	-2.96 (7.452)	19.60 (6.357)	-2.31 (2.838)
	Median	18.60	-1.20	18.80	-0.80	17.80	-3.50
	Min; Max	14.2; 31.6	-8.1; 14.2	12.5; 28.6	-17.4; 6.5	13.0; 32.4	-5.8; 2.0
Bilirubin Screening (umol/L)	n (missing) 7 (0)			7 (0)		7 (0)	
	Mean (SD)	13.11 (6.544)		13.00 (5.778)		11.81 (3.250)	
	Median	8.70		11.00		10.70	
	Min; Max	6.9; 23.6		6.3; 20.7		9.0; 18.5	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Aspartate Aminotransf (Day -1) erase (U/L)	Period 3/ n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	24.03 (3.929)		18.82 (4.032)		17.45 (4.269)		20.44 (5.099)	
	Median	24.25		17.80		17.25		19.10	
	Min; Max	19.3; 29.1		14.2; 25.3		12.1; 24.4		12.1; 31.5	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	22.51 (4.597)	-0.49 (5.202)	19.36 (3.547)	-3.00 (2.966)	17.01 (3.269)	-4.19 (3.417)	19.90 (5.309)	-2.08 (5.054)
	Median	20.90	0.60	17.50	-1.00	17.70	-3.70	18.70	-2.20
	Min; Max	18.2; 30.2	-8.1; 8.4	15.6; 25.3	-6.8; -0.5	11.6; 21.6	-9.5; 0.9	11.6; 32.4	-17.4; 14.2
Bilirubin (umol/L)	Screening	n (missing)	7 (0)	7 (0)		7 (0)		42 (0)	
	Mean (SD)	13.09 (4.524)		19.64 (5.799)		10.39 (4.419)		13.51 (5.670)	
	Median	12.50		19.40		7.50		12.15	
	Min; Max	7.2; 22.0		10.4; 26.8		6.1; 16.1		6.1; 26.8	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Bilirubin (umol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	15.17 (5.707)		11.57 (4.207)		14.06 (5.700)	
		Median	17.80		11.30		14.90	
		Min; Max	8.0; 21.2		6.8; 19.6		5.1; 21.6	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	11.84 (6.906)		12.95 (5.582)		11.43 (3.591)	
		Median	9.80		11.80		11.70	
		Min; Max	5.8; 26.8		6.9; 21.6		5.0; 16.3	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
Mean (SD)		11.69 (4.301)		12.38 (5.716)		10.94 (2.330)		
Median		10.50		12.30		11.70		
	Min; Max	7.2; 18.2		4.6; 20.5		7.9; 14.2		

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Bilirubin (umol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	11.64 (3.767)		15.86 (6.284)		11.94 (5.004)		13.37 (5.170)	
		Median	11.20		15.80		10.80		12.20	
		Min; Max	7.0; 17.1		7.1; 25.7		6.4; 21.2		5.1; 25.7	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	14.92 (4.848)		15.43 (4.085)		11.18 (5.354)		12.89 (5.113)	
		Median	14.95		16.35		11.50		12.25	
		Min; Max	7.8; 20.3		8.4; 20.2		4.9; 19.6		4.9; 26.8	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	13.68 (5.230)		14.58 (4.440)		9.12 (3.013)		12.03 (4.362)	
		Median	13.85		13.75		10.20		11.65	
		Min; Max	5.1; 21.4		10.2; 21.2		5.2; 12.6		4.6; 21.4	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)		
			Observed	Change	Observed	Change	Observed	Change	
Bilirubin (µmol/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	
		Mean (SD)	11.41 (7.651)	-1.70 (1.974)	13.03 (6.216)	0.03 (3.714)	9.94 (2.094)	-1.87 (3.727)	
		Median	7.10	-2.30	10.50	1.60	10.10	-2.00	
		Min; Max	3.8; 23.7	-4.9; 0.3	6.6; 24.4	-4.4; 4.3	7.5; 13.8	-8.3; 4.4	
Calcium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		
		Mean (SD)	2.384 (0.104)		2.366 (0.069)		2.394 (0.083)		
		Median	2.380		2.340		2.380		
		Min; Max	2.19; 2.53		2.26; 2.47		2.31; 2.56		
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		
			Mean (SD)	2.420 (0.095)		2.347 (0.091)		2.359 (0.099)	
			Median	2.450		2.340		2.340	
Min; Max			2.27; 2.57		2.19; 2.45		2.24; 2.51		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

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Dosage Form Proportionality of Levothyroxine New Formulations (50 µg, 100 µg, and 200 µg Tablets) in Fasted State

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Bilirubin (umol/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	12.49 (5.930)	-0.60 (5.299)	14.04 (8.338)	-5.60 (5.893)	10.01 (3.028)	-0.37 (4.215)	11.82 (5.820)	-1.69 (4.476)
		Median	15.60	-2.40	11.30	-5.90	9.90	-0.20	10.35	-2.15
		Min; Max	4.8; 20.1	-5.8; 7.1	4.6; 30.1	-11.9; 4.0	5.9; 13.8	-6.1; 7.0	3.8; 30.1	-11.9; 7.1
Calcium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	2.416 (0.085)		2.419 (0.087)		2.380 (0.083)		2.393 (0.083)	
		Median	2.430		2.430		2.390		2.400	
	Min; Max	2.27; 2.52		2.30; 2.53		2.30; 2.50		2.19; 2.56		
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	2.366 (0.063)		2.327 (0.060)		2.363 (0.114)		2.364 (0.088)	
Median		2.400		2.330		2.370		2.350		
Min; Max	2.29; 2.43		2.24; 2.42		2.21; 2.52		2.19; 2.57			

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine; Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)			
			Observed	Change	Observed	Change	Observed	Change		
Calcium (mmol/L)	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)			
		Mean (SD)	2.399 (0.067)		2.360 (0.109)		2.320 (0.109)			
		Median	2.380		2.390		2.280			
		Min; Max	2.32; 2.49		2.19; 2.47		2.22; 2.54			
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)			
		Mean (SD)	2.400 (0.040)		2.343 (0.058)		2.310 (0.089)			
		Median	2.400		2.355		2.290			
		Min; Max	2.33; 2.45		2.26; 2.40		2.22; 2.47			
	Follow-Up	n (missing)	7 (0)		7 (0)		7 (0)		7 (0)	
		Mean (SD)	2.350 (0.096)		-0.034 (0.056)		2.286 (0.095)		-0.080 (0.091)	
		Median	2.350		-0.020		2.300		-0.100	
		Min; Max	2.17; 2.44		-0.10; 0.06		2.12; 2.41		-0.22; 0.07	
						2.18; 2.42		-0.19; 0.09		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Calcium (mmol/L)	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	2.392 (0.028)		2.377 (0.077)		2.320 (0.080)		2.361 (0.084)	
		Median	2.380		2.390		2.320		2.380	
		Min; Max	2.37; 2.44		2.28; 2.46		2.20; 2.41		2.19; 2.54	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	2.395 (0.077)		2.323 (0.033)		2.378 (0.058)		2.358 (0.068)	
		Median	2.365		2.325		2.365		2.360	
		Min; Max	2.33; 2.54		2.27; 2.36		2.32; 2.49		2.22; 2.54	
	Follow-Up	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	42 (0)
		Mean (SD)	2.370 (0.055)	-0.046 (0.073)	2.303 (0.060)	-0.116 (0.079)	2.326 (0.097)	-0.054 (0.069)	2.324 (0.084)	-0.069 (0.079)
		Median	2.390	-0.040	2.310	-0.120	2.370	-0.080	2.335	-0.075
		Min; Max	2.27; 2.42	-0.16; 0.06	2.24; 2.41	-0.24; 0.00	2.19; 2.42	-0.11; 0.07	2.12; 2.44	-0.24; 0.09

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Chloride (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	101.30 (1.793)		102.73 (1.288)		102.10 (2.366)	
		Median	101.30		102.50		101.40	
		Min; Max	99.2; 104.4		101.3; 105.2		99.8; 105.7	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	101.47 (1.953)		102.29 (1.592)		101.54 (2.322)	
		Median	101.40		102.00		101.90	
		Min; Max	98.7; 104.2		99.8; 104.6		97.6; 105.0	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	102.30 (1.118)		103.17 (2.202)		103.31 (1.899)	
		Median	102.30		102.50		103.10	
		Min; Max	100.3; 103.9		100.9; 106.6		100.9; 105.9	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Chloride (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	101.67 (1.365)		101.94 (1.722)		102.87 (1.730)		102.10 (1.729)	
		Median	101.70		102.60		103.00		102.30	
		Min; Max	99.9; 103.6		98.5; 103.7		99.7; 105.5		98.5; 105.7	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	103.07 (1.721)		103.34 (2.039)		103.51 (2.618)		102.54 (2.112)	
		Median	103.50		102.50		103.40		102.45	
		Min; Max	99.9; 105.1		101.4; 106.9		99.0; 107.0		97.6; 107.0	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	102.43 (1.360)		102.10 (1.661)		103.43 (1.733)		102.79 (1.660)	
		Median	102.05		102.75		103.00		102.70	

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;
 Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.
 Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine
 Treatment C: 3 tablets of 200 µg of levothyroxine

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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	101.4; 104.9		99.2; 103.4		102.0; 106.7		99.2; 106.7	

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;
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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Chloride (mmol/L)	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	102.21 (2.789)		101.82 (1.804)		103.50 (1.265)	
		Median	101.90		102.00		103.70	
	Min; Max	96.9; 105.5		99.6; 104.2		101.1; 104.8		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	104.36 (2.915)	3.06 (3.250)	103.26 (2.625)	0.53 (2.533)	103.47 (2.052)	1.37 (2.821)
Median		104.90	3.30	104.60	0.00	103.80	2.60	
Min; Max	99.4; 107.6	-0.6; 8.1	99.5; 105.6	-3.0; 4.0	99.8; 106.5	-1.7; 4.1		
Creatine Kinase (IU/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	82.17 (20.550)		131.46 (108.114)		99.44 (30.827)	
		Median	87.70		100.20		90.00	
		Min; Max	55.3; 105.8		50.6; 372.7		65.7; 158.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Chloride (mmol/L)	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	102.75 (2.664)		103.22 (1.221)		102.53 (2.288)		102.68 (2.042)	
		Median	103.40		103.50		102.85		103.30	
	Min; Max	98.7; 106.4		101.1; 104.7		99.2; 105.5		96.9; 106.4		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	104.17 (1.080)	2.50 (1.832)	102.36 (2.480)	0.41 (2.339)	105.91 (2.620)	3.04 (2.237)	103.92 (2.489)	1.82 (2.632)
Median		104.10	3.00	102.50	1.00	106.10	2.90	104.25	2.25	
Min; Max	102.5; 105.6	0.1; 5.3	99.5; 105.7	-2.5; 4.5	101.9; 109.3	-0.9; 6.3	99.4; 109.3	-3.0; 8.1		
Creatine Kinase (IU/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	86.94 (27.679)		83.09 (28.253)		152.56 (141.858)		105.94 (76.302)	
		Median	87.60		84.70		97.70		91.00	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	48.4; 129.8		48.2; 133.6		59.5; 461.4		48.2; 461.4	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Creatine Kinase (IU/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	85.00 (17.460)		97.97 (41.368)		131.61 (133.630)	
		Median	88.60		82.30		71.20	
		Min; Max	58.3; 105.0		50.2; 174.2		63.2; 426.0	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	79.29 (26.967)		92.93 (22.999)		841.40 (1964.162)	
		Median	77.50		91.80		85.80	
		Min; Max	41.0; 121.8		70.1; 132.9		60.7; 5294.5	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	91.99 (29.239)		118.27 (85.937)		210.00 (218.338)	
		Median	92.60		88.20		84.90	
		Min; Max	46.6; 136.2		67.4; 291.3		48.9; 642.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Creatine Kinase (IU/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	91.91 (33.207)		92.40 (44.008)		182.50 (165.048)		113.57 (92.433)	
		Median	88.60		82.10		120.10		85.80	
	Min; Max	48.7; 153.4		58.2; 188.8		63.4; 536.9		48.7; 536.9		
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	101.88 (64.351)		98.68 (37.631)		137.22 (115.434)		237.61 (844.518)	
		Median	81.70		89.75		87.75		84.55	
	Min; Max	59.5; 230.4		63.5; 163.0		64.8; 364.9		41.0; 5294.5		
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	127.80 (88.591)		87.68 (25.790)		99.78 (39.127)		124.08 (110.156)	
		Median	104.45		84.40		81.20		86.85	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	55.0; 298.1		50.1; 117.1		61.9; 153.4		46.6; 642.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Creatine Kinase (IU/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	99.73 (36.604)	17.56 (23.880)	140.79 (76.212)	9.33 (77.707)	100.03 (56.508)	0.59 (26.311)
		Median	112.30	17.40	140.60	10.00	90.00	-7.10
		Min; Max	41.5; 136.9	-22.7; 48.1	48.4; 251.5	-121.2; 99.2	47.5; 213.2	-20.3; 55.2
Creatinine (umol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	60.84 (11.472)		64.06 (12.577)		62.06 (12.357)	
		Median	59.90		59.30		64.80	
		Min; Max	44.1; 79.6		49.2; 81.2		46.2; 76.8	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	63.10 (11.358)		67.77 (13.359)		64.49 (12.653)	
		Median	63.60		58.80		66.60	
		Min; Max	45.1; 79.6		56.6; 86.1		50.6; 80.8	

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;
 Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.
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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Creatine Kinase (IU/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	100.66 (47.188)	13.71 (27.137)	80.09 (30.645)	-3.00 (22.231)	89.04 (21.739)	-63.51 (133.047)	101.72 (49.143)	-4.22 (67.902)
		Median	81.70	13.10	73.00	-1.60	84.90	-17.70	92.40	1.90
		Min; Max	49.0; 171.3	-34.3; 41.6	43.7; 123.1	-32.7; 31.5	66.8; 131.0	-361.2; 13.9	41.5; 251.5	-361.2; 99.2
Creatinine (umol/L)	Screening	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	66.39 (6.985)	64.57 (6.005)	62.90 (15.044)	63.47 (10.658)				
		Median	64.30	65.20	57.70	63.30				
		Min; Max	57.5; 76.4	55.8; 72.5	48.8; 89.8	44.1; 89.8				
Period 1/ (Day -1)	n (missing)	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	68.91 (8.007)	66.99 (6.057)	67.26 (13.816)	66.42 (10.732)				
		Median	66.00	69.20	59.60	65.70				
		Min; Max	61.3; 84.2	57.8; 72.8	55.4; 91.6	45.1; 91.6				

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)		
			Observed	Change	Observed	Change	Observed	Change	
Creatinine (umol/L)	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)		
		Mean (SD)	63.37 (13.739)		71.82 (17.091)		64.07 (12.148)		
		Median	59.00		71.35		66.80		
	Min; Max	45.5; 80.0		51.6; 91.9		47.6; 77.6			
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)		
		Mean (SD)	63.37 (14.907)		71.45 (12.565)		63.83 (12.765)		
		Median	59.80		69.30		65.10		
	Min; Max	45.7; 88.0		56.0; 89.9		48.7; 78.9			
	Follow-Up	n (missing)	7 (0)		7 (0)		7 (0)		
		Mean (SD)	59.57 (12.495)		-1.27 (3.821)		66.13 (13.552)		2.07 (4.765)
Median		57.60		-0.20		59.80		0.80	
Min; Max	44.1; 77.3		-8.3; 4.4		49.7; 88.0		-5.2; 10.4		
						64.16 (13.388)		2.10 (3.650)	
						66.60		1.60	
						47.4; 83.2		-3.3; 9.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit)	Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Creatinine (umol/L)	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	69.55 (6.953)		67.12 (7.939)		68.38 (10.554)		67.19 (11.547)	
		Median	68.25		64.75		66.05		66.50	
		Min; Max	60.0; 79.0		60.0; 80.9		55.8; 84.1		45.5; 91.9	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	67.98 (8.871)		64.12 (5.972)		66.85 (13.840)		66.13 (11.553)	
		Median	66.10		64.40		62.30		64.40	
		Min; Max	58.2; 83.4		55.9; 72.9		52.1; 88.6		45.7; 89.9	
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	66.97 (10.816)	0.59 (4.938)	65.39 (8.236)	0.81 (5.376)	66.77 (11.066)	3.87 (5.415)	64.83 (11.291)	1.36 (4.700)
		Median	66.40	2.10	63.10	2.30	64.00	5.30	64.20	1.70
		Min; Max	53.2; 81.7	-7.7; 6.9	56.4; 78.5	-9.5; 6.0	53.1; 82.1	-7.7; 9.4	44.1; 88.0	-9.5; 10.4

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;
 Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.
 Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine
 Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Creatinine Clearance (mL/min/1.73m ²)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	116.3 (13.49)		105.6 (9.32)		109.4 (13.07)	
		Median	119.0		104.0		106.0	
		Min; Max	97; 136		92; 120		93; 133	
Direct Bilirubin (umol/L)	Screening	n (missing)	1 (0)		1 (0)			
		Mean (SD)	4.10 ()		5.50 ()			
		Median	4.10		5.50			
	Min; Max	4.1; 4.1		5.5; 5.5				
	Period 1/ (Day -1)	n (missing)	1 (0)				1 (0)	
		Mean (SD)	3.50 ()				3.20 ()	
Median		3.50				3.20		
		Min; Max	3.5; 3.5			3.2; 3.2		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Creatinine Clearance (mL/min/1.73m ²)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	103.4 (13.89)		106.3 (13.20)		117.0 (28.66)		109.7 (16.32)	
		Median	98.0		114.0		109.0		107.0	
		Min; Max	93; 133		91; 120		93; 179		91; 179	
		Direct Bilirubin (umol/L)	n (missing)	1 (0)		3 (0)				6 (0)
Direct Bilirubin (umol/L)	Screening	Mean (SD)	4.90 ()		4.40 (0.608)				4.62 (0.634)	
		Median	4.90		4.10				4.50	
		Min; Max	4.9; 4.9		4.0; 5.1				4.0; 5.5	
		Period 1/ (Day -1)	n (missing)		1 (0)		1 (0)			4 (0)
		Mean (SD)			4.10 ()		4.00 ()		3.70 (0.424)	
	Median			4.10		4.00		3.75		

Baseline defined as Screening for Follow-Up results.
 Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.
 Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;
 Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.
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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics Min; Max	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
				4.1; 4.1		4.0; 4.0		3.2; 4.1	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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 Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Direct Bilirubin (umol/L)	n (missing)	1 (0)		1 (0)			
Period 2/ (Day -1)	Mean (SD)	4.70 ()		3.60 ()			
	Median	4.70		3.60			
	Min; Max	4.7; 4.7		3.6; 3.6			
Period 3/ (Day -1)	n (missing)						
	Mean (SD)						
	Median						
	Min; Max						
Follow-Up	n (missing)	1 (0)	1 (0)	1 (0)	1 (0)		
	Mean (SD)	3.50 ()	-0.60 ()	4.30 ()	-1.20 ()		
	Median	3.50	-0.60	4.30	-1.20		
	Min; Max	3.5; 3.5	-0.6; -0.6	4.3; 4.3	-1.2; -1.2		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

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Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)		
			Observed	Change	Observed	Change	Observed	Change	Observed	Change	
Direct Bilirubin (umol/L)	Period 2/ (Day -1)	n (missing)							2	(0)	
		Mean (SD)							4.15	(0.778)	
		Median							4.15		
		Min; Max							3.6; 4.7		
	Period 3/ (Day -1)	n (missing)	1 (0)		1 (0)				2	(0)	
		Mean (SD)	4.00 (0)		3.60 (0)				3.80	(0.283)	
		Median	4.00		3.60				3.80		
		Min; Max	4.0; 4.0		3.6; 3.6				3.6; 4.0		
	Follow-Up	n (missing)			1 (0)	1 (0)			3	(0)	3 (0)
		Mean (SD)			4.20 (0)	0.20 (0)			4.00	(0.436)	-0.53
		Median			4.20	0.20			4.20	(0.702)	-0.60
		Min; Max			4.2; 4.2	0.2; 0.2			3.5; 4.3	-1.2; 0.2	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
		Observed	Change	Observed	Change	Observed	Change
Gamma Screening	n (missing)	7 (0)		7 (0)		7 (0)	
Glutamyl Transferase (U/L)	Mean (SD)	22.41 (15.379)		17.19 (8.464)		21.41 (14.067)	
	Median	18.20		14.40		18.70	
	Min; Max	13.3; 56.7		10.0; 34.3		11.7; 51.6	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
	Mean (SD)	19.94 (7.893)		16.31 (8.445)		21.19 (13.749)	
	Median	18.40		13.30		19.40	
	Min; Max	13.2; 36.4		8.9; 33.2		9.7; 50.0	
Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
	Mean (SD)	19.40 (8.377)		18.00 (9.202)		21.66 (15.974)	
	Median	16.10		13.10		18.50	
	Min; Max	12.5; 35.7		11.6; 34.1		9.0; 55.6	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Gamma Glutamyl Transferase (U/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	14.44 (2.405)		21.60 (13.858)		13.79 (3.513)		18.47 (10.836)	
		Median	14.10		13.70		14.40		14.65	
		Min; Max	11.2; 18.7		9.6; 47.8		8.4; 18.4		8.4; 56.7	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	14.09 (2.536)		20.37 (11.917)		14.33 (4.265)		17.70 (8.958)	
		Median	15.50		13.20		15.10		15.30	
		Min; Max	10.3; 16.6		9.9; 42.6		8.7; 20.6		8.7; 50.0	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	13.62 (2.127)		21.57 (15.892)		13.85 (4.200)		18.15 (10.591)	
	Median	13.75		13.45		13.20		14.20		

Baseline defined as Screening for Follow-Up results.

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Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

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Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	11.0; 15.9		10.8; 50.8		8.3; 19.7		8.3; 55.6	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Gamma Glutamyl Transferase (U/L)	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	19.54 (6.796)		17.43 (8.349)		17.84 (8.620)	
		Median	18.90		12.90		16.10	
	Min; Max	11.9; 30.3		11.7; 32.0		10.1; 34.2		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	18.99 (7.020)	-3.43 (11.411)	15.64 (6.530)	-1.54 (3.079)	19.80 (11.559)	-1.61 (2.640)
Median		18.50	-0.30	13.70	-1.50	16.50	-1.60	
Min; Max	10.9; 28.8	-27.9; 8.7	8.5; 26.4	-7.9; 1.2	11.9; 44.9	-6.7; 1.2		
Glucose (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	4.383 (0.483)		4.677 (0.495)		4.421 (0.336)	
	Median	4.290		4.580		4.400		
	Min; Max	3.87; 5.21		4.11; 5.63		3.80; 4.89		

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit)	Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Gamma Glutamyl Transferase (U/L)	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	14.08 (2.616)		20.65 (18.220)		13.68 (3.081)		17.28 (9.091)	
		Median	13.50		13.05		13.90		13.90	
		Min; Max	11.7; 19.1		10.2; 57.4		9.0; 17.6		9.0; 57.4	
Follow-Up		n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	14.44 (2.362)	0.00 (2.179)	19.96 (16.402)	-1.64 (4.995)	13.44 (4.208)	-0.34 (2.790)	17.05 (9.104)	-1.43 (5.310)
		Median	14.10	-0.20	11.90	-2.10	13.50	-0.60	14.00	-0.75
		Min; Max	11.7; 18.7	-3.2; 3.6	9.9; 55.3	-7.6; 7.5	7.8; 18.5	-4.9; 3.9	7.8; 55.3	-27.9; 8.7
Glucose (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	4.617 (0.351)		4.374 (0.325)		4.594 (0.275)		4.511 (0.382)	
		Median	4.510		4.420		4.650		4.500	
		Min; Max	4.25; 5.12		4.01; 4.87		4.18; 4.95		3.80; 5.63	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Glucose (mmol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	4.643 (0.440)		4.966 (0.621)		4.647 (0.535)	
		Median	4.720		4.950		4.510	
		Min; Max	4.04; 5.37		4.27; 5.82		4.08; 5.66	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	4.573 (0.514)		4.967 (0.430)		4.610 (0.359)	
		Median	4.580		4.990		4.490	
		Min; Max	3.96; 5.47		4.43; 5.44		4.20; 5.24	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	4.739 (0.468)		4.965 (0.209)		4.526 (0.312)	
		Median	4.800		4.985		4.590	
		Min; Max	4.13; 5.43		4.66; 5.19		4.03; 4.89	

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Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

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Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Glucose (mmol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	4.703 (0.298)		4.439 (0.278)		4.700 (0.443)		4.683 (0.452)	
		Median	4.730		4.490		4.760		4.605	
		Min; Max	4.28; 5.16		4.10; 4.88		4.14; 5.18		4.04; 5.82	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	4.477 (0.361)		4.462 (0.191)		4.765 (0.344)		4.639 (0.397)	
		Median	4.605		4.420		4.840		4.560	
		Min; Max	3.98; 4.81		4.23; 4.70		4.26; 5.24		3.96; 5.47	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	4.760 (0.370)		4.667 (0.185)		5.013 (0.315)		4.771 (0.350)	
		Median	4.890		4.585		5.145		4.780	
		Min; Max	4.11; 5.10		4.51; 5.01		4.56; 5.34		4.03; 5.43	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Glucose (mmol/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	4.680 (0.276)	0.297 (0.340)	4.829 (0.532)	0.151 (0.374)	4.706 (0.416)	0.284 (0.587)
		Median	4.580	0.290	4.590	-0.060	4.540	0.110
		Min; Max	4.46; 5.28	-0.24; 0.82	4.19; 5.62	-0.28; 0.70	4.35; 5.43	-0.47; 1.09
Indirect Bilirubin (umol/L)	Screening	n (missing)	1 (0)	1 (0)				
		Mean (SD)	19.50 ()		27.60 ()			
		Median	19.50		27.60			
	Min; Max	19.5; 19.5		27.6; 27.6				
	Period 1/ (Day -1)	n (missing)	1 (0)				1 (0)	
		Mean (SD)	17.70 ()				18.40 ()	
Median		17.70				18.40		
Min; Max	17.7; 17.7				18.4; 18.4			

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Glucose (mmol/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
		Mean (SD)	4.750 (0.204)	0.133 (0.382)	4.626 (0.278)	0.251 (0.360)	4.697 (0.522)	0.103 (0.361)	4.715 (0.373)	0.203 (0.392)
		Median	4.690	0.330	4.670	0.180	4.770	0.020	4.670	0.225
		Min; Max	4.52; 5.16	-0.60; 0.43	4.30; 5.05	-0.12; 0.95	3.97; 5.59	-0.35; 0.64	3.97; 5.62	-0.60; 1.09
Indirect Bilirubin (umol/L)	Screening	n (missing)	1 (0)		3 (0)				6 (0)	
		Mean (SD)	17.10 ()		20.47 (2.491)				20.93 (3.854)	
		Median	17.10		21.70				20.60	
	Min; Max	17.1; 17.1		17.6; 22.1				17.1; 27.6		
	Period 1/ (Day -1)	n (missing)			1 (0)		1 (0)		4 (0)	
		Mean (SD)			21.60 ()		17.20 ()		18.73 (1.979)	
Median				21.60		17.20		18.05		
Min; Max			21.6; 21.6		17.2; 17.2		17.2; 21.6			

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Indirect Bilirubin (umol/L)	Period 2/ (Day -1)	n (missing)	1 (0)		1 (0)			
		Mean (SD)	22.10 ()		18.00 ()			
		Median	22.10		18.00			
		Min; Max	22.1; 22.1		18.0; 18.0			
	Period 3/ (Day -1)	n (missing)						
		Mean (SD)						
		Median						
		Min; Max						
	Follow-Up	n (missing)	1 (0)	1 (0)	1 (0)	1 (0)		
		Mean (SD)	20.20 ()	0.70 ()	20.10 ()	-7.50 ()		
Median		20.20	0.70	20.10	-7.50			
Min; Max		20.2; 20.2	0.7; 0.7	20.1; 20.1	-7.5; -7.5			

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB; Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine; Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)		
			Observed	Change	Observed	Change	Observed	Change	Observed	Change	
Indirect Bilirubin (umol/L)	Period 2/ (Day -1)	n (missing)							2	(0)	
		Mean (SD)							20.05	(2.899)	
		Median Min; Max							20.05	18.0; 22.1	
	Period 3/ (Day -1)	n (missing)	1 (0)		1 (0)				2	(0)	
		Mean (SD)	17.40 ()		17.60 ()				17.50	(0.141)	
		Median Min; Max	17.40 17.4; 17.4		17.60 17.6; 17.6				17.50	17.4; 17.6	
	Follow-Up	n (missing)			1 (0)	1 (0)			3	(0)	3 (0)
		Mean (SD)			25.90 ()	3.80 ()			22.07	-1.00	(3.320) (5.839)
		Median Min; Max			25.90 25.9; 25.9	3.80 3.8; 3.8			20.20	0.70	20.1; 25.9 -7.5; 3.8

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Lactate Dehydrogenase (IU/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	152.94 (18.368)		167.59 (17.139)		174.54 (18.018)	
		Median	152.30		167.80		176.90	
		Min; Max	130.8; 189.7		141.1; 195.3		145.7; 195.5	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	151.96 (15.903)		166.24 (13.572)		176.06 (13.310)	
		Median	156.00		170.30		175.20	
		Min; Max	132.3; 176.4		147.0; 184.3		155.6; 193.9	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	147.23 (27.776)		158.58 (18.729)		178.97 (39.548)	
		Median	149.10		159.40		172.30	
		Min; Max	114.1; 197.5		131.1; 185.9		148.1; 264.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Lactate	Screening n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
Dehydrogenase (IU/L)	Mean (SD)	168.34 (37.049)		154.57 (14.491)		161.71 (12.139)		163.28 (21.304)	
	Median	165.50		156.40		159.80		159.50	
	Min; Max	123.9; 217.7		136.3; 172.8		142.5; 176.3		123.9; 217.7	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	169.41 (28.842)		162.14 (12.005)		170.61 (17.548)		166.07 (18.355)	
	Median	165.70		159.70		169.70		165.50	
	Min; Max	133.1; 214.5		152.0; 186.0		148.7; 196.0		132.3; 214.5	
Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	160.20 (23.026)		154.03 (13.658)		156.00 (20.474)		159.38 (26.209)	
	Median	173.00		150.65		158.10		157.05	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	130.6; 178.8		137.3; 171.7		128.4; 179.8		114.1; 264.0	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Lactate Dehydrogenase (IU/L)	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	158.43 (29.898)		169.18 (15.972)		159.54 (17.484)	
		Median	162.90		167.55		151.10	
	Min; Max	119.5; 207.8		149.0; 192.3		138.4; 184.0		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	150.14 (26.410)	-2.80 (13.409)	165.74 (17.922)	-1.84 (22.405)	155.33 (18.139)	-19.21 (9.933)
Median		150.50	-3.80	168.70	-9.10	150.70	-20.00	
Min; Max	111.1; 190.6	-19.7; 21.7	144.0; 186.5	-18.9; 44.2	136.8; 186.5	-30.7; -4.5		
Potassium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	4.207 (0.245)		4.217 (0.260)		4.253 (0.357)	
		Median	4.290		4.260		4.250	
		Min; Max	3.84; 4.52		3.89; 4.66		3.64; 4.76	

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)		
			Observed	Change	Observed	Change	Observed	Change	Observed	Change	
Lactate Dehydrogenase (IU/L)	Period 3/	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)		
		Mean (SD)	171.33 (32.456)		153.98 (13.751)		149.23 (19.084)		160.22 (22.489)		
		Median	181.65		154.45		148.20		159.85		
	Min; Max	121.2; 211.1		133.6; 173.2		127.7; 174.6		119.5; 211.1			
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)	
		Mean (SD)	165.60 (28.247)	-2.74 (17.578)	144.43 (11.359)	-10.14 (8.313)	148.11 (11.155)	-13.60 (10.245)	154.89 (20.522)	-8.39 (15.105)	
		Median	173.80	4.00	145.20	-9.20	150.10	-9.70	150.65	-9.15	
		Min; Max	121.3; 194.0	-28.3; 17.7	127.1; 160.7	-21.7; 1.1	134.9; 167.6	-32.3; -0.8	111.1; 194.0	-32.3; 44.2	
	Potassium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
			Mean (SD)	4.021 (0.344)		4.299 (0.265)		4.519 (0.298)		4.253 (0.316)	
Median		4.030		4.210		4.550		4.260			
Min; Max		3.61; 4.48		4.01; 4.85		4.18; 4.97		3.61; 4.97			

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1: ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine

Treatment C: 3 tablets of 200 µg of levothyroxine

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Potassium (mmol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	4.203 (0.357)		4.291 (0.212)		4.284 (0.126)	
		Median	4.290		4.270		4.340	
		Min; Max	3.64; 4.57		4.05; 4.59		4.03; 4.39	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	4.386 (0.347)		4.153 (0.350)		4.349 (0.202)	
		Median	4.420		4.040		4.310	
		Min; Max	3.99; 4.81		3.78; 4.77		4.08; 4.61	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
Mean (SD)		4.354 (0.412)		4.258 (0.376)		4.277 (0.138)		
Median		4.520		4.250		4.300		
	Min; Max	3.85; 4.88		3.66; 4.66		4.14; 4.54		

Baseline defined as Screening for Follow-Up results.

Max: Maximum Value; Min: Minimum Value; N: The number of subjects dosed with each treatment, or the number of subjects in the safety population for the total summary; n: Number of subjects in specific laboratory tests.

Treatment Sequence 1:ABC; Treatment Sequence 2: BCA; Treatment Sequence 3: CAB; Treatment Sequence 4: ACB;

Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

Treatment A: 12 tablets of 50 µg of levothyroxine; Treatment B: 6 tablets of 100 µg of levothyroxine
Treatment C: 3 tablets of 200 µg of levothyroxine/project24/ep/blinded/e210898_merc/stats/versioncontrol/primary/scripts/program/main/TFL programs/Tables/Table
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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Potassium (mmol/L)	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	4.283 (0.320)		4.264 (0.364)		4.373 (0.345)		4.283 (0.286)	
		Median	4.310		4.300		4.470		4.315	
		Min; Max	3.87; 4.73		3.74; 4.91		3.65; 4.70		3.64; 4.91	
	Period 2/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	4.243 (0.201)		4.177 (0.343)		4.363 (0.223)		4.283 (0.282)	
		Median	4.230		4.075		4.340		4.240	
		Min; Max	4.01; 4.55		3.87; 4.76		4.13; 4.75		3.78; 4.81	
	Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
		Mean (SD)	4.408 (0.237)		4.355 (0.257)		4.573 (0.217)		4.368 (0.288)	
		Median	4.370		4.275		4.505		4.325	
		Min; Max	4.16; 4.73		4.11; 4.77		4.38; 4.98		3.66; 4.98	

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Potassium (mmol/L)	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	4.330 (0.373)	0.123 (0.353)	4.344 (0.250)	0.127 (0.290)	4.334 (0.227)	0.081 (0.438)
		Median	4.290	0.230	4.300	0.050	4.240	0.100
		Min; Max	3.88; 4.79	-0.42; 0.58	4.09; 4.76	-0.21; 0.61	4.09; 4.67	-0.52; 0.53
Protein (mL/min/1.73m ²)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	70.70 (2.704)		69.93 (2.055)		73.06 (2.713)	
		Median	71.90		69.50		72.00	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	72.17 (4.191)		70.36 (3.012)		71.03 (4.977)	
		Median	71.20		70.00		69.10	
		Min; Max	67.6; 78.9		66.6; 74.9		64.7; 78.8	

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Potassium (mmol/L) Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	4.409 (0.158)	0.387 (0.420)	4.330 (0.343)	0.031 (0.319)	4.551 (0.261)	0.033 (0.194)	4.383 (0.273)	0.130 (0.346)
	Median	4.420	0.310	4.310	-0.050	4.590	0.080	4.350	0.090
	Min; Max	4.25; 4.67	-0.14; 1.06	3.96; 4.89	-0.22; 0.69	4.12; 4.85	-0.31; 0.24	3.88; 4.89	-0.52; 1.06
Protein (mL/min/1.73m ²) Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	72.90 (3.349)		70.40 (3.370)		69.67 (3.538)		71.11 (3.131)	
	Median	74.20		70.30		68.80		71.05	
	Min; Max	68.8; 77.0		65.2; 75.0		65.8; 75.6		65.2; 77.0	
Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
	Mean (SD)	73.76 (2.629)		69.14 (3.221)		70.37 (3.135)		71.14 (3.705)	
	Median	74.60		70.60		69.90		70.50	
	Min; Max	68.4; 76.4		62.6; 71.9		67.5; 76.3		62.6; 78.9	

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Treatment Sequence 5: BAC; Treatment Sequence 6: CBA.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit)	Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Protein (mL/min/1.7 (Day -1) 3m2)	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	71.51 (3.107)		71.13 (2.323)		69.80 (4.516)	
		Median	70.40		70.20		68.60	
		Min; Max	67.3; 76.3		68.7; 74.4		64.9; 76.6	
	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	72.09 (3.621)		70.83 (2.183)		69.04 (3.618)	
		Median	71.80		71.35		70.50	
		Min; Max	67.2; 77.2		67.2; 73.1		61.6; 72.4	
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	68.47 (1.953)	-2.23 (2.593)	68.94 (4.329)	-0.99 (3.605)	69.79 (4.967)	-3.27 (4.796)
		Median	68.90	-2.10	70.00	0.60	70.60	-4.20
		Min; Max	65.9; 71.2	-6.0; 1.6	61.4; 74.6	-7.3; 2.2	60.7; 76.4	-8.6; 4.4

Baseline defined as Screening for Follow-Up results.

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
Protein Period 2/ (mL/min/1.7 (Day -1) 3m2)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	72.17 (0.891)		70.88 (3.120)		68.38 (2.967)		70.65 (3.121)	
	Median	72.00		70.45		68.95		70.55	
	Min; Max	71.0; 73.3		67.4; 74.4		64.0; 72.6		64.0; 76.6	
Period 3/ (Day -1)	n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Mean (SD)	73.17 (2.620)		68.07 (2.455)		70.68 (3.549)		70.64 (3.366)	
	Median	73.75		68.10		71.40		70.85	
	Min; Max	68.7; 75.8		64.7; 70.9		66.5; 75.1		61.6; 77.2	
Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	42 (0)	42 (0)
	Mean (SD)	72.41 (1.939)	-0.49 (3.481)	67.11 (2.763)	-3.29 (3.319)	68.74 (2.140)	-0.93 (1.860)	69.25 (3.457)	-1.86 (3.384)
	Median	72.90	-1.00	67.40	-2.20	68.20	-0.60	69.40	-1.75
	Min; Max	69.5; 74.8	-4.1; 6.0	63.1; 71.3	-7.6; 0.2	66.4; 72.1	-3.5; 2.4	60.7; 76.4	-8.6; 6.0

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Dosage Form Proportionality of Levothyroxine New Formulations (50 µg, 100 µg, and 200 µg Tablets) in Fasted State

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Sodium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	138.09 (1.860)		138.86 (1.253)		138.56 (1.804)	
		Median	138.30		139.10		139.30	
		Min; Max	134.7; 140.2		136.7; 140.0		136.1; 140.4	
	Period 1/ (Day -1)	n (missing)	7 (0)		7 (0)		7 (0)	
		Mean (SD)	137.64 (2.205)		137.07 (1.078)		137.00 (2.153)	
		Median	137.40		137.10		137.70	
		Min; Max	133.2; 139.7		135.7; 138.7		132.3; 138.5	
	Period 2/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	137.97 (1.170)		138.38 (1.023)		138.04 (1.290)	
		Median	138.40		138.40		137.60	
		Min; Max	136.3; 139.4		137.2; 140.1		136.8; 140.3	

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)Page 63 of 85
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Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
			Observed	Change	Observed	Change	Observed	Change	Observed	Change
Sodium (mmol/L)	Screening	n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	137.27 (2.094)		137.96 (1.522)		138.74 (0.954)		138.25 (1.622)	
		Median	137.20		137.80		138.70		138.25	
	Period 1/ (Day -1)	Min; Max	134.7; 140.5		136.2; 140.5		137.6; 140.5		134.7; 140.5	
		n (missing)	7 (0)		7 (0)		7 (0)		42 (0)	
		Mean (SD)	137.47 (2.152)		137.39 (1.485)		138.01 (1.671)		137.43 (1.758)	
	Period 2/ (Day -1)	Median	137.70		137.70		138.70		137.70	
		Min; Max	133.9; 140.0		135.7; 139.6		134.4; 139.2		132.3; 140.0	
		n (missing)	6 (0)		6 (0)		6 (0)		38 (0)	
	Period 2/ (Day -1)	Mean (SD)	136.97 (1.480)		137.20 (1.292)		138.43 (1.724)		137.84 (1.365)	
		Median	137.05		137.40		139.10		138.10	

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Laboratory Visit/ Test (Unit) Timepoint	Statistics	Treatment Sequence 4 (N=7)		Treatment Sequence 5 (N=7)		Treatment Sequence 6 (N=7)		Total (N=42)	
		Observed	Change	Observed	Change	Observed	Change	Observed	Change
	Min; Max	135.1; 138.7		135.0; 138.7		135.1; 139.6		135.0; 140.3	

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Table 15.3.5.1.2 Summary and Change from Baseline of Laboratory Data by Treatment and Time Point: Clinical Chemistry (Safety Population)

Laboratory Test (Unit)	Visit/ Timepoint	Statistics	Treatment Sequence 1 (N=7)		Treatment Sequence 2 (N=7)		Treatment Sequence 3 (N=7)	
			Observed	Change	Observed	Change	Observed	Change
Sodium (mmol/L)	Period 3/ (Day -1)	n (missing)	7 (0)		6 (0)		7 (0)	
		Mean (SD)	136.93 (2.213)		137.25 (0.883)		137.61 (1.128)	
		Median	136.50		136.85		138.00	
	Min; Max	134.2; 140.5		136.4; 138.6		135.7; 139.0		
	Follow-Up	n (missing)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)	7 (0)
		Mean (SD)	139.40 (1.733)	1.31 (3.041)	138.34 (1.926)	-0.51 (1.244)	138.46 (1.275)	-0.10 (2.112)
Median		138.70	0.20	138.80	-1.10	138.40	-0.40	
Min; Max	137.8; 142.6	-2.4; 5.9	135.3; 140.7	-1.7; 1.7	136.8; 140.7	-2.5; 2.8		
Thyrotropin Screening (mU/L)	n (missing)	7 (0)		7 (0)		7 (0)		
		Mean (SD)	1.431 (0.566)		1.156 (0.434)		1.584 (0.514)	
		Median	1.630		0.890		1.630	
		Min; Max	0.64; 1.95		0.72; 1.72		0.86; 2.16	

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