

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Benralizumab (Fasenra®)

AstraZeneca GmbH

Modul 4 A – Anhang 4-G

Add-on-Therapie bei erwachsenen und jugendlichen Patient:innen im Alter von 12 Jahren und älter mit einem Körpergewicht von mindestens 35 kg mit unzureichend kontrolliertem hypereosinophilem Syndrom ohne eine erkennbare, nicht-hämatologische sekundäre Ursache

Ergänzende Analysen

Stand: 14.07.2026

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – SF-36

Subscale / Category	Benralizumab N=67 n (%)	Placebo N=66 n (%)	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
PCS improvement >= 3.4 points	37 (55.2)	25 (37.9)	1.46 (1.00; 2.12)	0.0450	2.02 (1.01; 4.04)	0.0450	0.173 (0.006; 0.340)	0.0417
MCS improvement >= 4.6 points	30 (44.8)	20 (30.3)	1.48 (0.94; 2.32)	0.0849	1.86 (0.91; 3.80)	0.0849	0.145 (-0.018; 0.307)	0.0812
Physical Functioning improvement >= 4.3 points	19 (28.4)	15 (22.7)	1.25 (0.69; 2.24)	0.4567	1.35 (0.61; 2.95)	0.4567	0.056 (-0.092; 0.204)	0.4555
Role Physical improvement >= 3.4 points	38 (56.7)	25 (37.9)	1.50 (1.03; 2.17)	0.0296	2.15 (1.07; 4.30)	0.0296	0.188 (0.022; 0.355)	0.0267
Bodily Pain improvement >= 6.2 points	30 (44.8)	23 (34.8)	1.28 (0.84; 1.96)	0.2423	1.52 (0.75; 3.05)	0.2423	0.099 (-0.066; 0.265)	0.2397
General Health improvement >= 7.2 points	26 (38.8)	12 (18.2)	2.13 (1.18; 3.86)	0.0085	2.85 (1.29; 6.32)	0.0085	0.206 (0.057; 0.355)	0.0068
Vitality improvement >= 6.2 points	29 (43.3)	18 (27.3)	1.59 (0.98; 2.56)	0.0534	2.04 (0.98; 4.21)	0.0534	0.160 (0.000; 0.320)	0.0499
Social Functioning improvement >= 6.9 points	25 (37.3)	23 (34.8)	1.07 (0.68; 1.68)	0.7673	1.11 (0.55; 2.26)	0.7673	0.025 (-0.139; 0.188)	0.7672
Role Emotional improvement >= 4.5 points	26 (38.8)	16 (24.2)	1.60 (0.95; 2.70)	0.0708	1.98 (0.94; 4.18)	0.0708	0.146 (-0.010; 0.301)	0.0671
Mental Health improvement >= 6.2 points	23 (34.3)	20 (30.3)	1.13 (0.69; 1.86)	0.6197	1.20 (0.58; 2.49)	0.6197	0.040 (-0.119; 0.199)	0.6193

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) – p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – PROMIS

	Benralizumab N=67	Placebo N=66						
Subscale / Category	n (%)	n (%)	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
Improvement >= 6 points	33 (49.3)	22 (33.3)	1.48 (0.97; 2.25)	0.0623	1.94 (0.96; 3.91)	0.0623	0.159 (-0.006; 0.324)	0.0588
Improvement >= 10 points	26 (38.8)	13 (19.7)	1.97 (1.11; 3.49)	0.0155	2.59 (1.18; 5.64)	0.0155	0.191 (0.040; 0.342)	0.0132
Improvement >= 13 points	21 (31.3)	7 (10.6)	2.96 (1.35; 6.48)	0.0034	3.85 (1.51; 9.83)	0.0034	0.207 (0.074; 0.341)	0.0024

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) – p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – PGIS Baseline

Subscale / Category	Benralizumab	Placebo	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
	N=67 n (%)	N=65 n (%)						
No symptoms	4 (6.0)	4 (6.2)	0.97 (0.25; 3.72)	0.9647	0.97 (0.23; 4.05)	0.9647	-0.002 (-0.083; 0.080)	0.9647
Very mild symptoms	10 (14.9)	8 (12.3)	1.21 (0.51; 2.88)	0.6613	1.25 (0.46; 3.40)	0.6613	0.026 (-0.091; 0.143)	0.6607
Mild symptoms	10 (14.9)	11 (16.9)	0.88 (0.40; 1.93)	0.7537	0.86 (0.34; 2.19)	0.7537	-0.020 (-0.145; 0.105)	0.7538
Moderate symptoms	30 (44.8)	19 (29.2)	1.53 (0.96; 2.43)	0.0646	1.96 (0.96; 4.03)	0.0646	0.155 (-0.007; 0.318)	0.0608
Severe symptoms	10 (14.9)	21 (32.3)	0.46 (0.24; 0.90)	0.0185	0.37 (0.16; 0.86)	0.0185	-0.174 (-0.316; -0.032)	0.0165
Very severe symptoms	3 (4.5)	2 (3.1)	1.46 (0.25; 8.43)	0.6734	1.48 (0.24; 9.14)	0.6734	0.014 (-0.051; 0.079)	0.6724

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) - p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – PGIS Week 24

Subscale / Category	Benralizumab	Placebo	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
	N=64 n (%)	N=59 n (%)						
No symptoms	17 (26.6)	11 (18.6)	1.42 (0.73; 2.79)	0.2954	1.58 (0.67; 3.72)	0.2954	0.079 (-0.068; 0.226)	0.2908
Very mild symptoms	17 (26.6)	16 (27.1)	0.98 (0.55; 1.76)	0.9446	0.97 (0.44; 2.16)	0.9446	-0.006 (-0.162; 0.151)	0.9446
Mild symptoms	13 (20.3)	14 (23.7)	0.86 (0.44; 1.67)	0.6474	0.82 (0.35; 1.93)	0.6474	-0.034 (-0.181; 0.112)	0.6479
Moderate symptoms	13 (20.3)	12 (20.3)	1.00 (0.50; 2.01)	0.9971	1.00 (0.41; 2.40)	0.9971	-0.000 (-0.143; 0.142)	0.9971
Severe symptoms	4 (6.2)	6 (10.2)	0.61 (0.18; 2.07)	0.4268	0.59 (0.16; 2.20)	0.4268	-0.039 (-0.137; 0.058)	0.4297
Very severe symptoms	0 (0.0)	0 (0.0)	NC	NC	NC	NC	NC	NC

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) - p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – PGIC Week 24

Subscale / Category	Benralizumab	Placebo	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
	N=64 n (%)	N=58 n (%)						
Much better	27 (42.2)	14 (24.1)	1.75 (1.02; 3.00)	0.0351	2.29 (1.05; 5.00)	0.0351	0.180 (0.017; 0.344)	0.0306
Considerably better	12 (18.8)	6 (10.3)	1.81 (0.73; 4.52)	0.1911	2.00 (0.70; 5.73)	0.1911	0.084 (-0.040; 0.208)	0.1827
Somewhat better	13 (20.3)	8 (13.8)	1.47 (0.66; 3.30)	0.3408	1.59 (0.61; 4.17)	0.3408	0.065 (-0.067; 0.198)	0.3353
No change	9 (14.1)	22 (37.9)	0.37 (0.19; 0.74)	0.0025	0.27 (0.11; 0.65)	0.0025	-0.239 (-0.390; -0.087)	0.0020
Somewhat worse	0 (0.0)	6 (10.3)	0.07 (0.00; 1.21)	0.0135	0.06 (0.00; 1.14)	0.0135	-0.103 (-0.182; -0.025)	0.0097
Considerably worse	3 (4.7)	2 (3.4)	1.36 (0.24; 7.85)	0.7303	1.38 (0.22; 8.55)	0.7303	0.012 (-0.058; 0.082)	0.7283
Much worse	0 (0.0)	0 (0.0)	NC	NC	NC	NC	NC	NC

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) – p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.1.1
Patient Reported Outcomes – Responder Analysis – PGIC Week 24 – Combined

Subscale / Category	Benralizumab	Placebo	RR (95% CI)	p-value	OR (95% CI)	p-value	RD (95% CI)	p-value
	N=64	N=58						
	n (%)	n (%)						
Improvement (somewhat/considerably/much better)	52 (81.2)	28 (48.3)	1.68 (1.26; 2.25)	0.0001	4.64 (2.06; 10.46)	0.0001	0.330 (0.170; 0.490)	0.0001
Deterioration (somewhat/considerably/much worse)	3 (4.7)	8 (13.8)	0.34 (0.09; 1.22)	0.0795	0.31 (0.08; 1.22)	0.0795	-0.091 (-0.194; 0.012)	0.0824

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of responders. PRO=Patient Reported Outcome. PGIC=Patient Global Impression of Change.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) – p(Placebo) with Wald 95% CI based on normal approximation.
P-values: RR and OR from chi-squared test; RD from z-test (normal approximation). All confidence intervals are at the 95% level.
PGIC Combined: Improvement = somewhat/considerably/much better. Deterioration = somewhat/considerably/much worse.

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HTA Adhoc Table 3.2.1							
Patient Reported Outcomes – Standardized Mean Difference (Hedges' g) at Week 24 – SF-36							
Endpoint / Domain	Benra n	Placebo n	Benralizumab (N=67)	Placebo (N=66)	Diff (95% CI)	p-value	Hedges' g (95% CI)
			LS Mean (95% CI)	LS Mean (95% CI)			
Physical Component Summary	64	58	6.7 (4.9; 8.5)	2.2 (0.3; 4.0)	4.54 (1.9; 7.1)	0.0008	0.615 (0.251; 0.979)
Mental Component Summary	64	58	5.3 (3.2; 7.3)	2.7 (0.5; 4.8)	2.60 (-0.4; 5.6)	0.0852	0.309 (-0.048; 0.666)
Physical Functioning	64	58	4.6 (2.9; 6.3)	0.2 (-1.5; 1.9)	4.40 (2.0; 6.8)	0.0004	0.645 (0.280; 1.009)
Role Physical	64	58	7.8 (5.8; 9.8)	2.8 (0.7; 4.8)	5.02 (2.1; 7.9)	0.0008	0.616 (0.252; 0.980)
Bodily Pain	64	58	7.0 (4.9; 9.1)	3.5 (1.2; 5.7)	3.54 (0.5; 6.6)	0.0238	0.402 (0.043; 0.761)
General Health	64	58	6.3 (4.4; 8.2)	2.6 (0.6; 4.6)	3.71 (0.9; 6.5)	0.0093	0.474 (0.113; 0.834)
Vitality	64	58	7.9 (5.8; 10.0)	3.4 (1.2; 5.6)	4.48 (1.4; 7.5)	0.0043	0.522 (0.161; 0.884)
Social Functioning	64	58	7.3 (5.4; 9.2)	4.5 (2.5; 6.5)	2.78 (0.0; 5.5)	0.0479	0.358 (0.000; 0.717)
Role Emotional	64	58	4.7 (2.4; 7.0)	1.4 (-1.0; 3.8)	3.32 (-0.1; 6.7)	0.0535	0.350 (-0.008; 0.709)
Mental Health	64	58	4.5 (2.5; 6.6)	1.7 (-0.5; 3.9)	2.83 (-0.2; 5.8)	0.0629	0.329 (-0.029; 0.687)

Hedges' g=Standardized Mean Difference with small sample correction. CI=Confidence Interval. LS=Least Squares. Diff=Difference.
Benra=Benralizumab. SF-36=Short Form 36 Health Survey. PROMIS=Patient-Reported Outcomes Measurement Information System.
N=Number of patients in treatment group (randomised). n=Number of patients with data at Week 24.
Diff (95% CI) and p-value from repeated measures ANCOVA model (Benralizumab – Placebo).
For SF-36, positive values favour Benralizumab. For PROMIS Fatigue, negative values favour Benralizumab (lower score = less fatigue).
All confidence intervals are at the 95% level.

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HTA Adhoc Table 3.2.1							
Patient Reported Outcomes – Standardized Mean Difference (Hedges' g) at Week 24 – PROMIS Fatigue							
Endpoint / Domain			Benralizumab	Placebo	Diff (95% CI)	p-value	Hedges' g (95% CI)
	Benra	Placebo	(N=67)	(N=66)			
	n	n	LS Mean (95% CI)	LS Mean (95% CI)			
PROMIS Fatigue Total Score	64	59	-8.6 (-10.6; -6.6)	-3.9 (-6.0; -1.8)	-4.72 (-7.6; -1.8)	0.0017	-0.570 (-0.931; -0.209)

Hedges' g=Standardized Mean Difference with small sample correction. CI=Confidence Interval. LS=Least Squares. Diff=Difference.
Benra=Benralizumab. SF-36=Short Form 36 Health Survey. PROMIS=Patient-Reported Outcomes Measurement Information System.
N=Number of patients in treatment group (randomised). n=Number of patients with data at Week 24.
Diff (95% CI) and p-value from repeated measures ANCOVA model (Benralizumab – Placebo).
For SF-36, positive values favour Benralizumab. For PROMIS Fatigue, negative values favour Benralizumab (lower score = less fatigue).
All confidence intervals are at the 95% level.

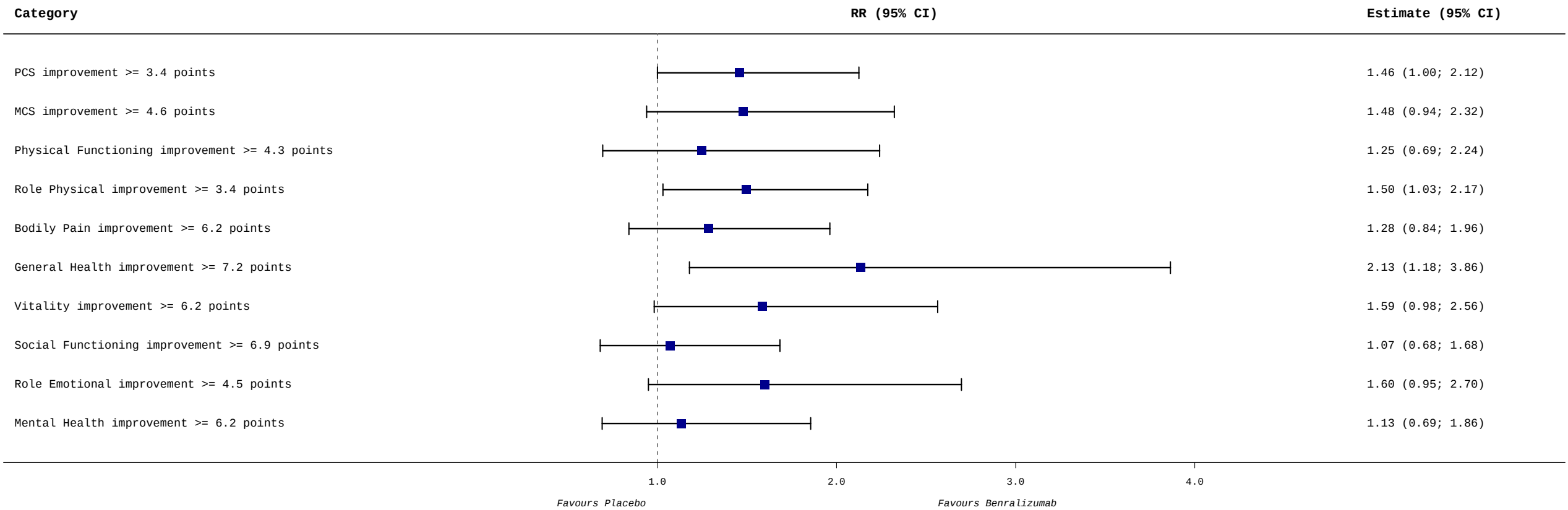
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HTA Adhoc Table 4.1.1						
Safety Endpoints – Overall						
AE category	Benralizumab	Placebo	RR (95% CI)	OR (95% CI)	RD (95% CI)	p-value
	N=67	N=66				
	n (%)	n (%)				
Any AE	43 (64.2)	44 (66.7)	0.96 (0.75; 1.23)	0.90 (0.44; 1.83)	-0.025 (-0.186; 0.137)	0.8289
Any severe AE	6 (9.0)	5 (7.6)	1.18 (0.38; 3.69)	1.20 (0.35; 4.14)	0.014 (-0.080; 0.107)	0.8453
Any SAE	5 (7.5)	5 (7.6)	0.99 (0.30; 3.24)	0.98 (0.27; 3.57)	-0.001 (-0.091; 0.088)	1.0000
AEs leading to discontinuation of IP	1 (1.5)	0 (0.0)	2.96 (0.12; 71.28)	3.00 (0.12; 74.98)	0.015 (-0.014; 0.044)	0.5285
AEs with outcome death	1 (1.5)	0 (0.0)	2.96 (0.12; 71.28)	3.00 (0.12; 74.98)	0.015 (-0.014; 0.044)	0.5285

NC=Not calculable (zero events in both groups). RR=Risk Ratio. OR=Odds Ratio. RD=Risk Difference. CI=Confidence Interval.
N=Number of patients in treatment group. n=Number of patients with at least one event. AE=Adverse Event. SAE=Serious Adverse Event. IP=Investigational Product.
RR and OR calculated using Wald method with 95% CI. A 0.5 continuity correction is applied when any cell contains zero events.
RD calculated as p(Benralizumab) – p(Placebo) with Wald 95% CI. P-value from Barnard's unconditional exact test (CSM), two-sided.
All confidence intervals are at the 95% level.

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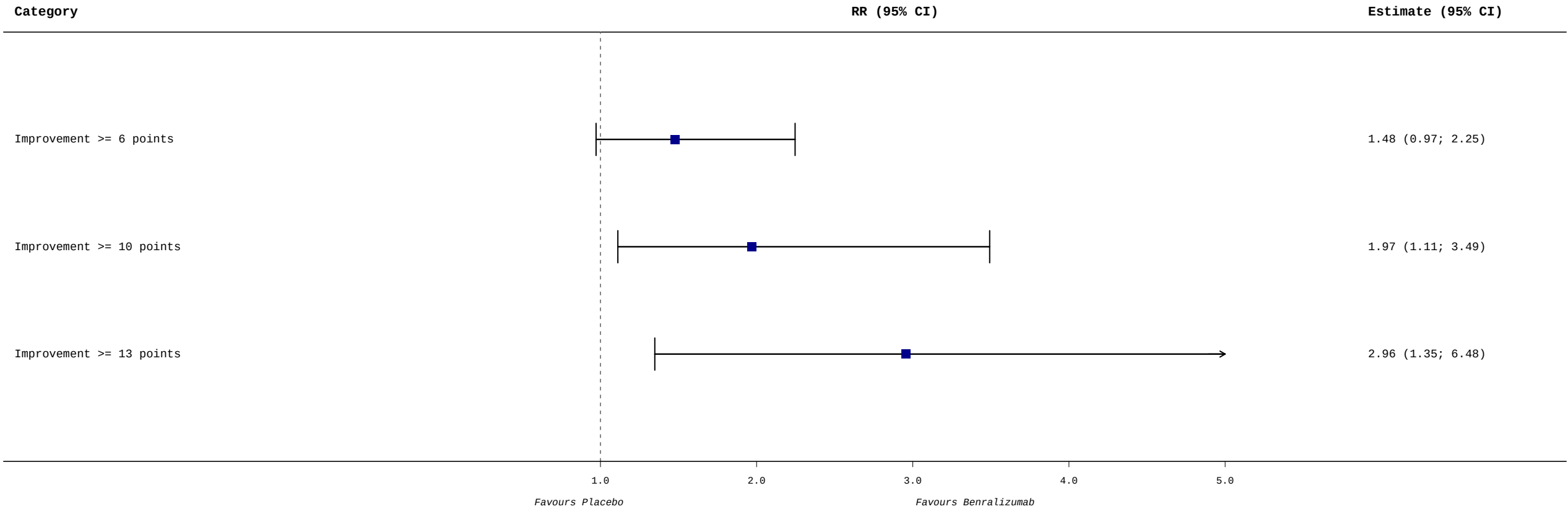
HTA Adhoc Figure 3.1.1
PRO Responder Analysis – Forest Plot of Risk Ratios – SF-36



RR=Risk Ratio (Wald method). CI=Confidence Interval. NC=Not calculable (zero events in both groups).
A 0.5 continuity correction is applied when any cell contains zero events. Dashed line at RR=1 indicates no effect.
All confidence intervals are at the 95% level. Arrows indicate CI extends beyond plot area.

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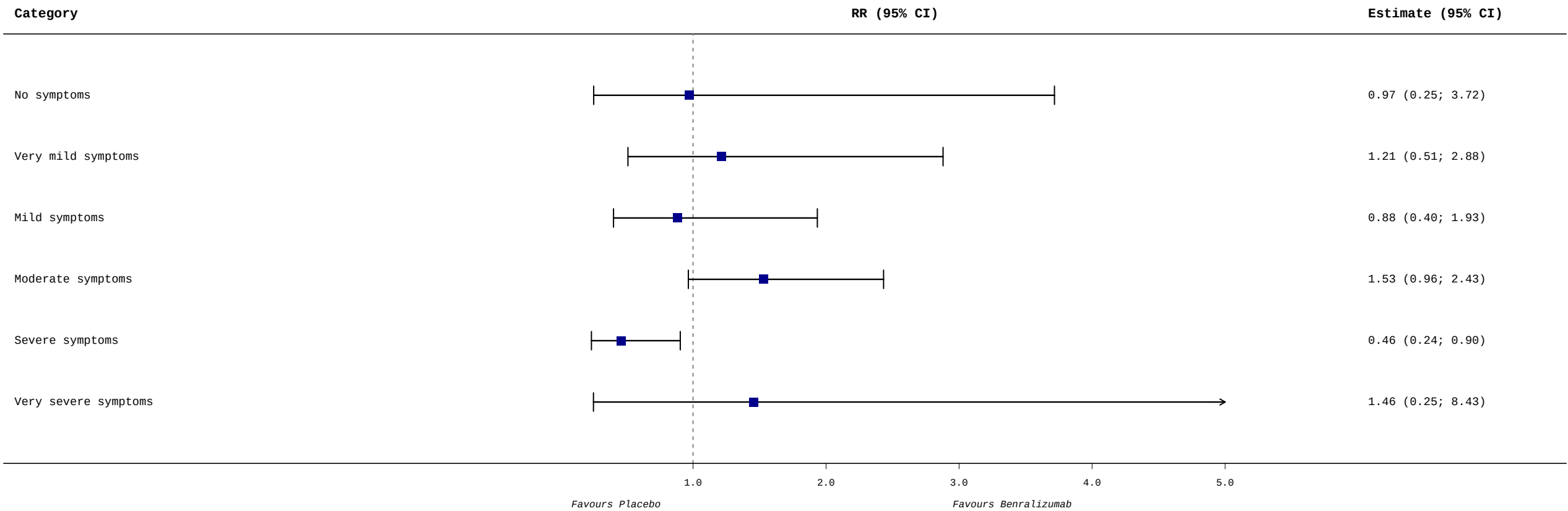
HTA Adhoc Figure 3.1.1
PRO Responder Analysis – Forest Plot of Risk Ratios – PROMIS



RR=Risk Ratio (Wald method). CI=Confidence Interval. NC=Not calculable (zero events in both groups).
A 0.5 continuity correction is applied when any cell contains zero events. Dashed line at RR=1 indicates no effect.
All confidence intervals are at the 95% level. Arrows indicate CI extends beyond plot area.

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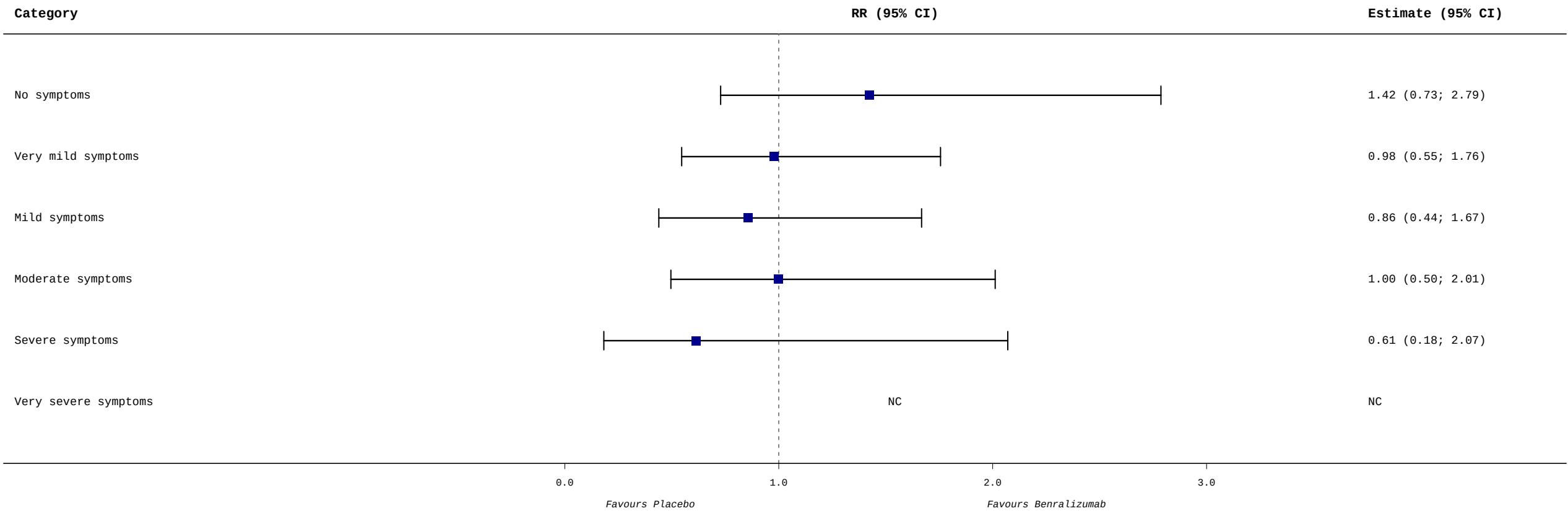
HTA Adhoc Figure 3.1.1
PRO Responder Analysis – Forest Plot of Risk Ratios – PGIS Baseline



RR=Risk Ratio (Wald method). CI=Confidence Interval. NC=Not calculable (zero events in both groups).
A 0.5 continuity correction is applied when any cell contains zero events. Dashed line at RR=1 indicates no effect.
All confidence intervals are at the 95% level. Arrows indicate CI extends beyond plot area.

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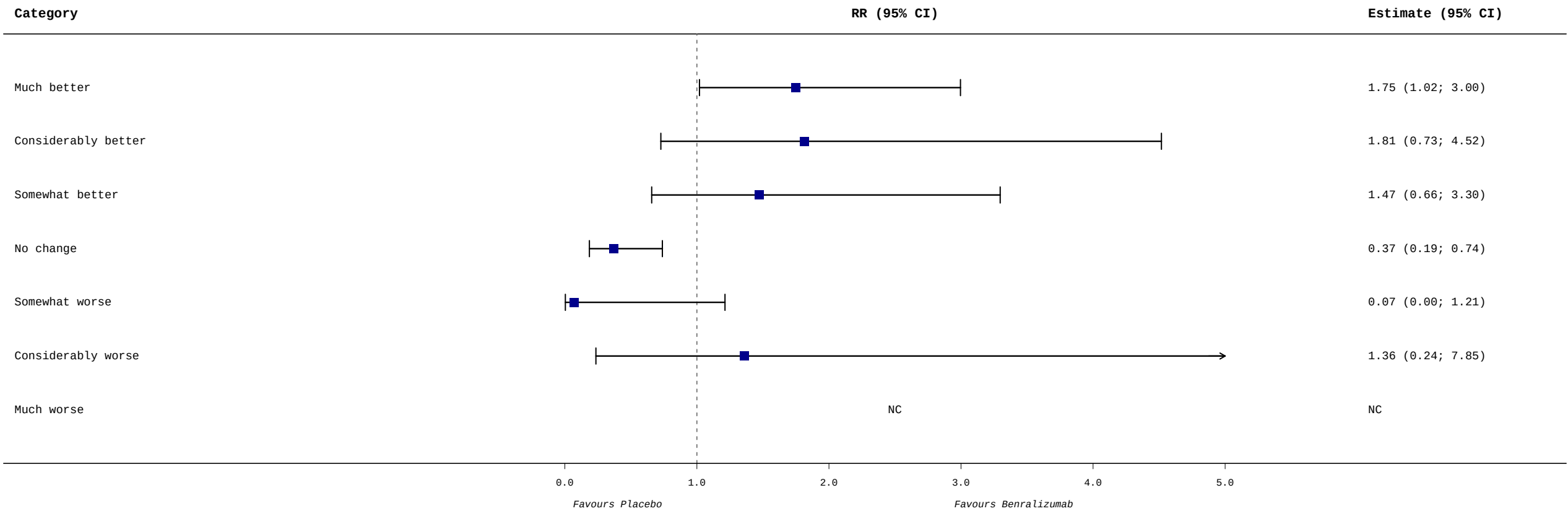
HTA Adhoc Figure 3.1.1
PRO Responder Analysis – Forest Plot of Risk Ratios – PGIS Week 24



RR=Risk Ratio (Wald method). CI=Confidence Interval. NC=Not calculable (zero events in both groups).
A 0.5 continuity correction is applied when any cell contains zero events. Dashed line at RR=1 indicates no effect.
All confidence intervals are at the 95% level. Arrows indicate CI extends beyond plot area.

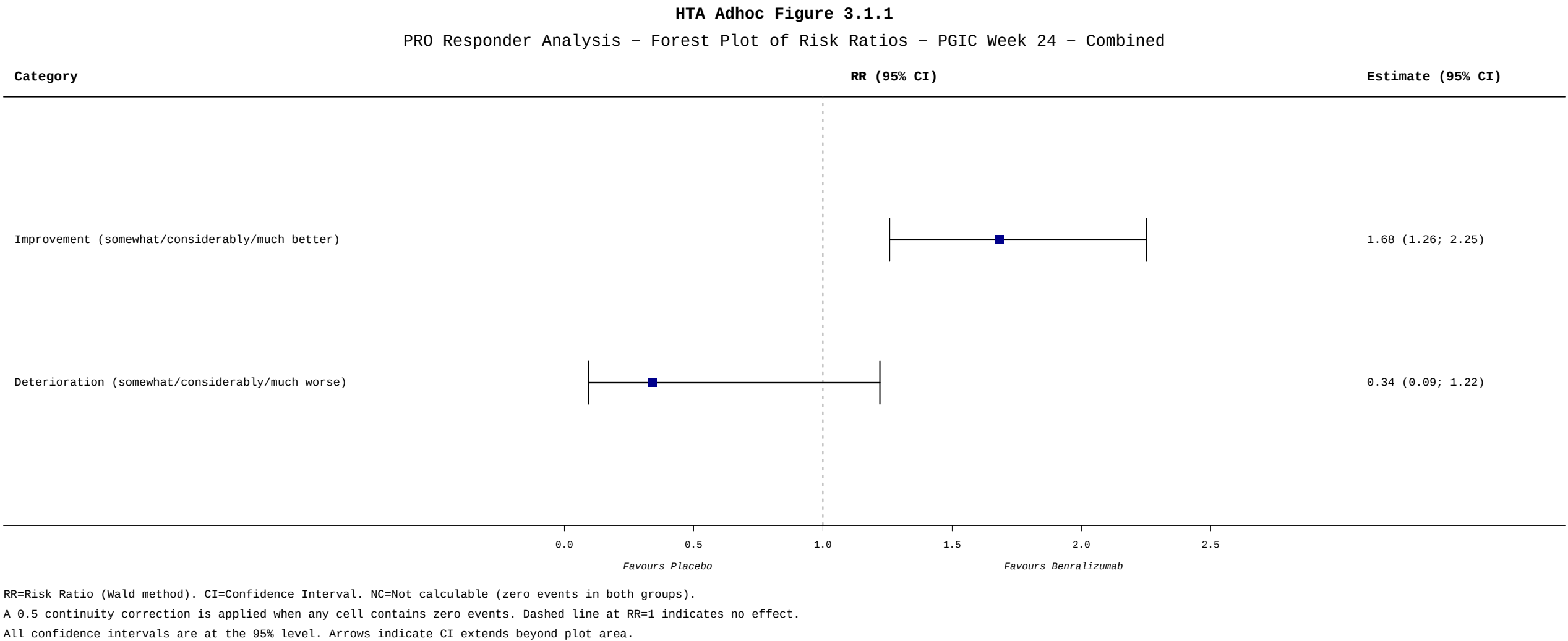
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HTA Adhoc Figure 3.1.1
PRO Responder Analysis – Forest Plot of Risk Ratios – PGIC Week 24

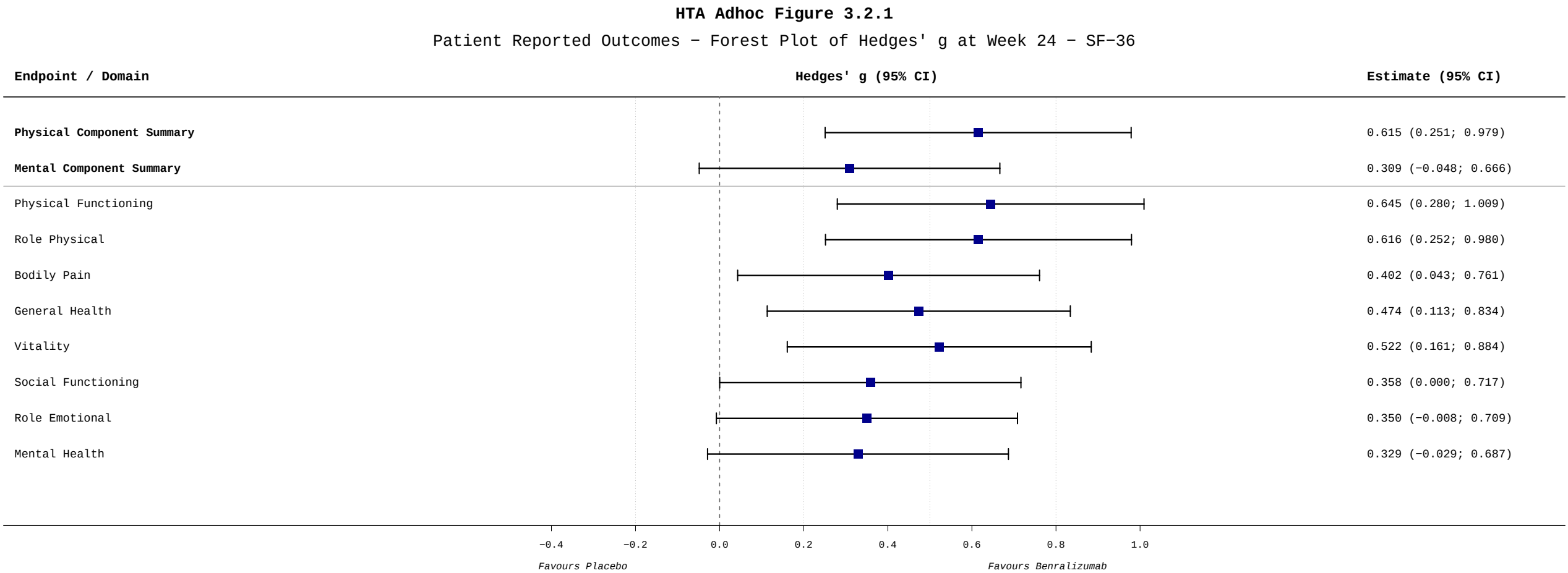


RR=Risk Ratio (Wald method). CI=Confidence Interval. NC=Not calculable (zero events in both groups).
A 0.5 continuity correction is applied when any cell contains zero events. Dashed line at RR=1 indicates no effect.
All confidence intervals are at the 95% level. Arrows indicate CI extends beyond plot area.

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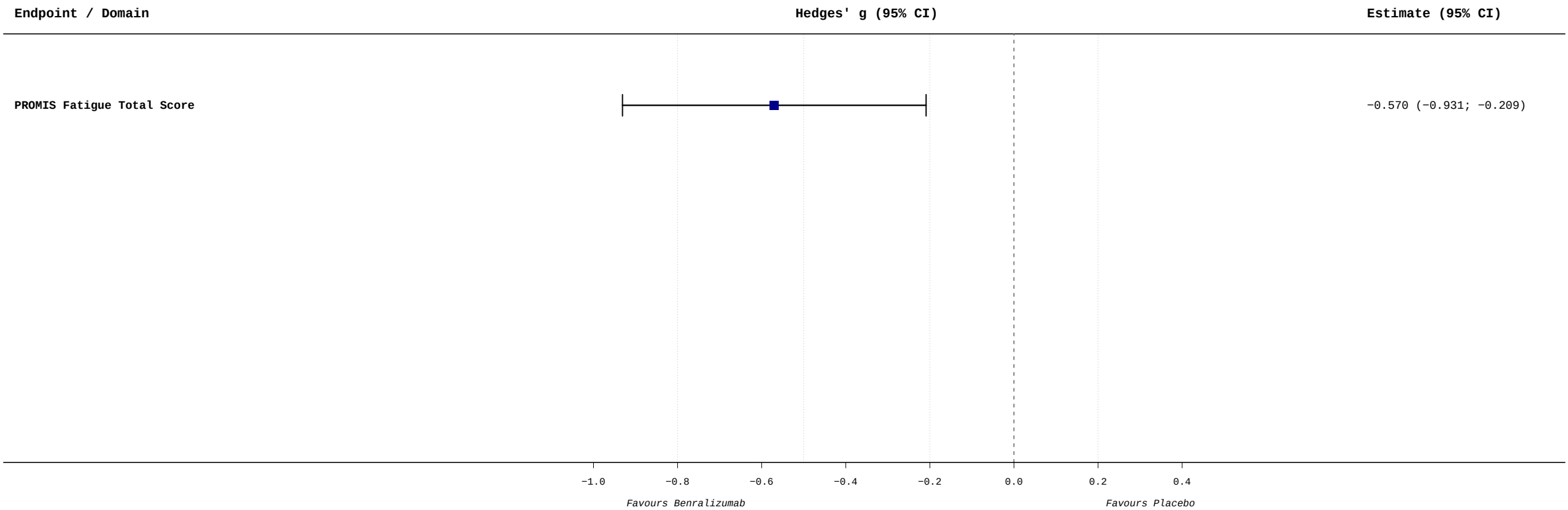
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Hedges' g=Standardized Mean Difference with small sample correction. CI=Confidence Interval.
Benra=Benralizumab. N=67 (Benralizumab), N=66 (Placebo) randomised. n=Number of patients with data at Week 24.
Dashed line at 0 indicates no effect. Dotted lines indicate Cohen's thresholds (0.2 small, 0.5 medium, 0.8 large).
Positive values favour Benralizumab.
All confidence intervals are at the 95% level.

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HTA Adhoc Figure 3.2.1
Patient Reported Outcomes – Forest Plot of Hedges' g at Week 24 – PROMIS Fatigue



Hedges' g=Standardized Mean Difference with small sample correction. CI=Confidence Interval.
Benra=Benralizumab. N=67 (Benralizumab), N=66 (Placebo) randomised. n=Number of patients with data at Week 24.
Dashed line at 0 indicates no effect. Dotted lines indicate Cohen's thresholds (0.2 small, 0.5 medium, 0.8 large).
Negative values favour Benralizumab (lower score = less fatigue).
All confidence intervals are at the 95% level.