Impact of the Follicular Lymphoma (FL) treatment continuum on a patients quality of life (QoL) in Europe (EU5)

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Disclosures

- Project funded by Janssen-Cilag GmbH
- Collaboration of Adelphi Real World and Janssen
- Haefliger B., Bacon T. are employees of Janssen
- Bacon T. holds stock of Johnson and Johnson
- Massey L., Rider A., Bailey A. are employees of Adelphi Real World

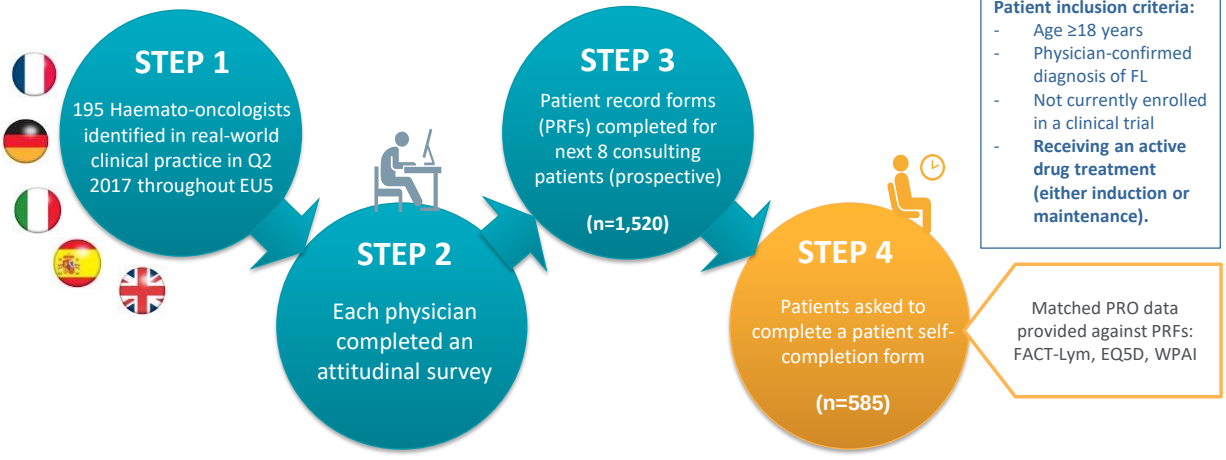
Background

- Non-Hodgkin lymphoma (NHL) is the 10th most common cancer worldwide, of which Follicular Lymphoma (FL) is a subtype[1].
  - The incidence of 1st and 2nd line FL patients is estimated to increase by 40% and 49% respectively from 2010 to 2020[1].
- Previous real world data suggests that relapsed patients are more likely to progress whilst on therapy[2]
- There is a **lack of real world evidence evaluating quality of life (QoL)** of FL patients and how factors including line of therapy change the outcome of patient QoL.

Objective

Investigate key factors that impact QoL for patients with FL across European countries (France, Germany, Italy, Spain and UK)

Methods



Patients completing the self-completion form are in significantly better health than the overall population

	Overall (n=1520)	PSC not completed (n=935)	PSC completed (n=585)	P-value (stats test)
Patient age (mean, SD)	65.5, 11.1	65.9, 11.0	65.1, 11.3	0.4355 (MW)
Time since diagnosis (days) (mean, SD)	1108.2, 1233.9	1167.9, 1281.2	1012.8, 1148.9	0.0056 (MW)
Grade (n, %)* Grade 1 Grade 2 Grade 3a Grade 3b	(n=1255) 120 (9.6) 523 (41.7) 439 (35.0) 173 (13.8)	(n=752) 80 (10.6) 309 (41.1) 270 (35.9) 93 (12.4)	(n=503) 40 (8.0) 214 (42.5) 169 (33.6) 80 (15.9)	0.1316 (CH)
Stage at initiation of current therapy* Stage I Stage II Stage III Stage IV	(n=1303) 61 (4.7) 191 (14.7) 532 (40.8) 519 (39.8)	(n=779) 30 (3.9) 105 (13.5) 317 (40.7) 327 (42.0)	(n=524) 31 (5.9) 86 (16.4) 215 (41.0) 192 (36.6)	0.0738 (CH)
ECOG score* 0 – Fully active 1 – Restricted activity 2 – Self-care only 3 – Limited self-care 4 – Completely disabled	(n=1515) 449 (29.6) 738 (48.7) 273 (18.0) 50 (3.3) 5 (0.3)	(n=932) 292 (31.3) 432 (46.4) 180 (19.3) 25 (2.7) 3 (0.3)	(n=583) 157 (26.9) 306 (52.5) 93 (16.0) 25 (4.3) 2 (0.3)	0.0376 (CH)
Number of comorbidities (mean, SD)	1.3, 1.4	1.3, 1.4	1.2, 1.4	0.0338 (MW)
Line of therapy (n, %)* 1 2 3 4+	 395 (26.0) 937 (61.6) 161 (10.6) 27 (1.8)	 215 (23.0) 594 (63.5) 103 (11.0) 23 (2.5)	 180 (30.8) 343 (58.6) 58 (9.9) 4 (0.7)	0.0009 (CH)
Response to treatment (n, %)* Responding to current treatment Refractory to treatment Response unknown at this time	274 (18.0) 92 (6.1) 103 (6.8)	148 (15.8) 76 (8.1) 52 (5.6)	126 (21.5) 16 (2.7) 51 (8.7)	0.0060 (FE) <0.0001 (FE) 0.0207 (FE)

*Bases vary based on response

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- **Patients completing the self completion form are in better health** than the overall population, namely
  - Shorter time since diagnosis
  - Different ECOG score
  - Fewer comorbidities
  - Fewer lines for treatment
  - Better response to treatment
- **Higher impact on QoL measures could be expected** in overall population

*Bases vary based on response

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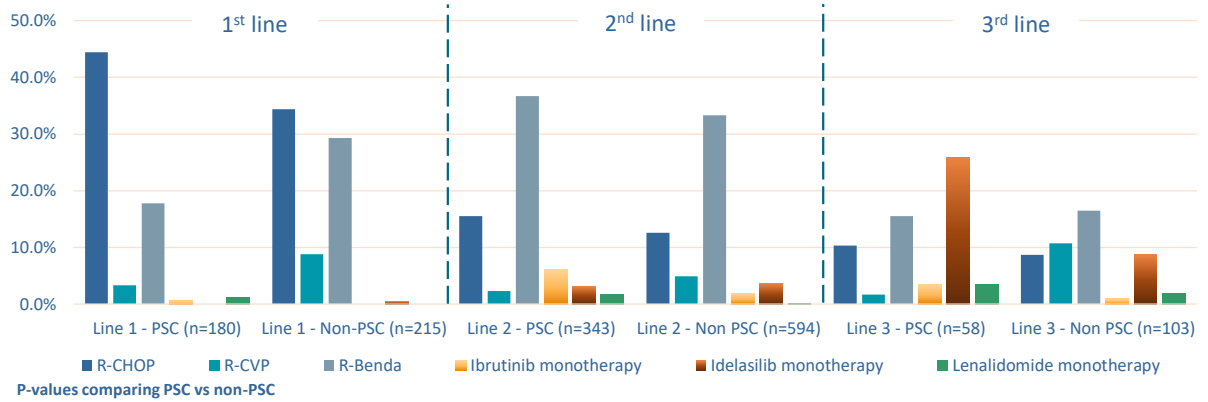
First line R-CHOP followed by BR and various treatments in later line



P-values comparing PSC vs non-PSC

	R-CHOP	R-CVP	R-Benda	Ibrutinib monotherapy	Idelalisib monotherapy	Lenalidomide monotherapy
1st line PSC vs non PSC	0.0491	0.0362	0.0092	0.4557	1.0000	0.2070
2nd line PSC vs non PSC	0.2368	0.0566	0.3183	0.0011	0.8543	0.0113
3rd line PSC vs non PSC	0.7812	0.0571	1.0000	0.2946	0.0052	0.6196

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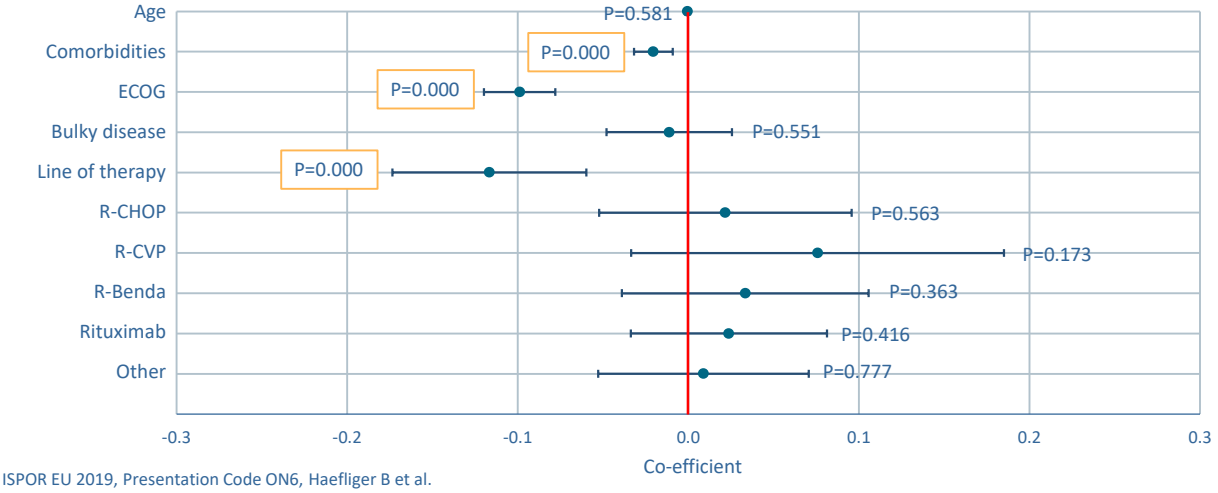
Patients with more comorbidities, higher ECOG score and higher line of therapy have significantly lower EQ5D outcomes

Multivariate regression between patient base line characteristics (covariates) and EQ5D (outcome)
Regression coefficient, n=580



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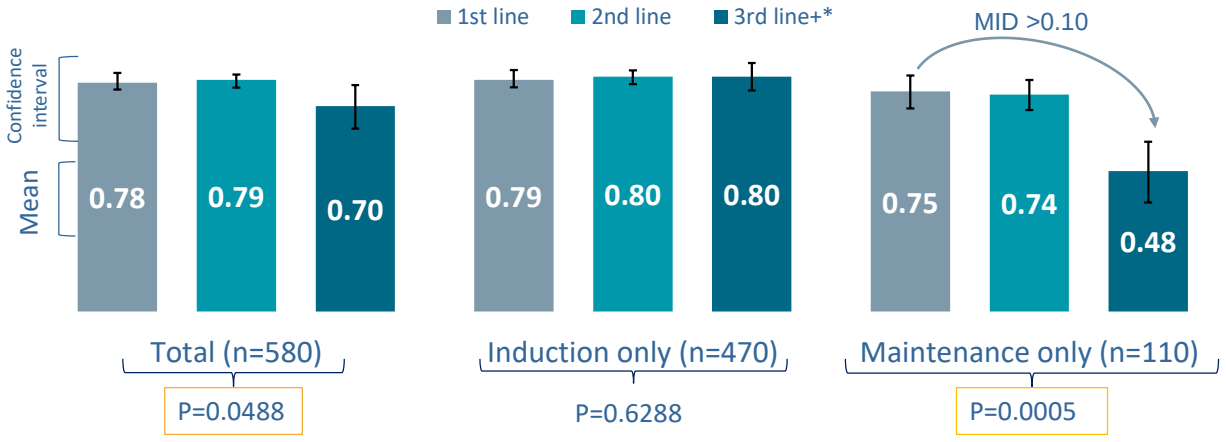
Maintenance therapy patients have worse EQ5D outcomes on later lines while induction patients have similar outcomes across lines

Weighted means between patient line of therapy and EQ5D score
Significant difference between lines, n=580



*Includes 3rd line and 4th line

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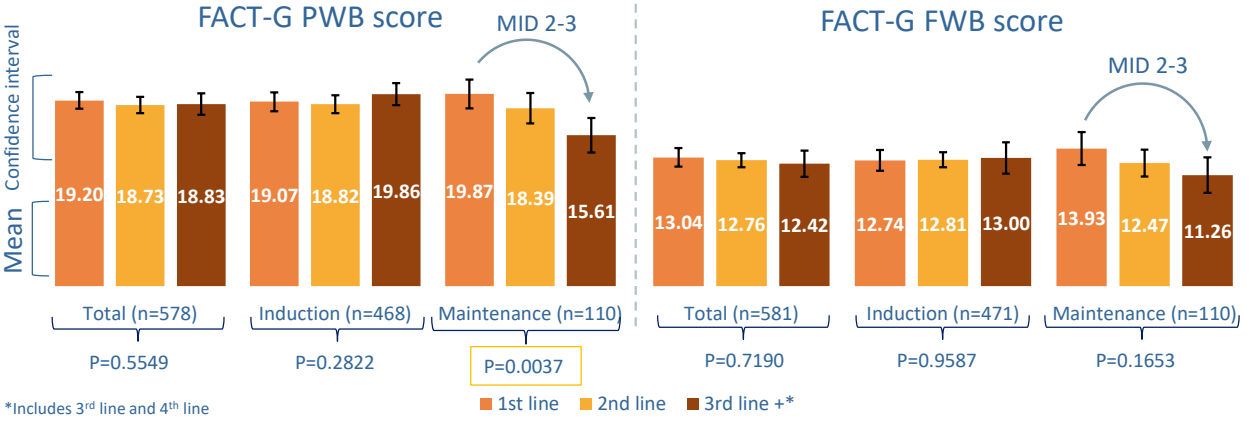
Both physical and functional wellbeing are impaired for later line patient in FACT-G, confirming EQ5D results

Weighted means between patient line of therapy and FACT-G physical and functional well-being scores
Significant difference between lines, n=580



*Includes 3rd line and 4th line

Note: Physical well-being (PWB), social well-being (SWB) and functional well-being (FWB) scores range from 0-28, emotional well-being (EWB) score ranges from 0-24. The higher the score, the better the QoL.

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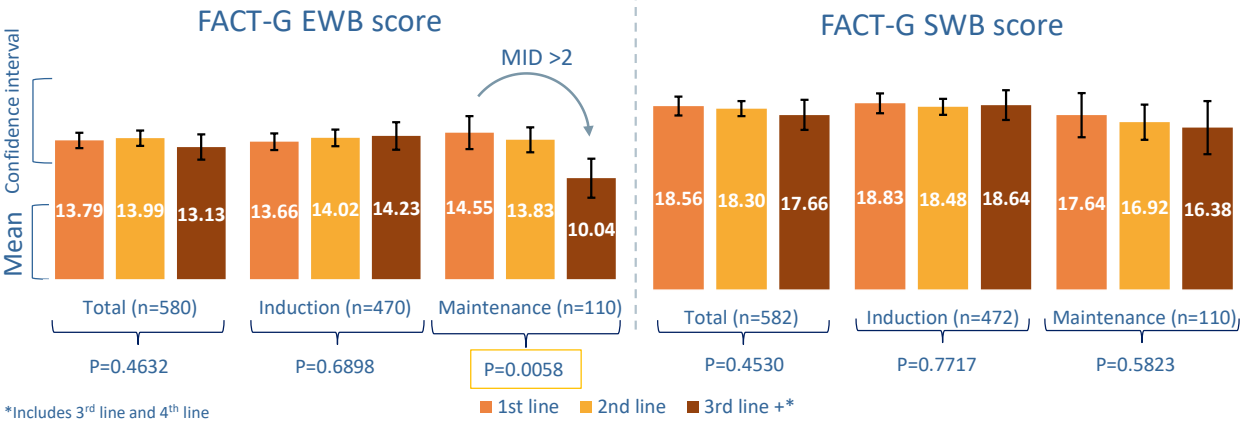
11

Later line maintenance patients have significantly lower emotional wellbeing but feel socially less impaired

Weighted means between patient line of therapy and FACT-G emotional and social well-being scores
Significant difference between lines, n=580



*Includes 3rd line and 4th line

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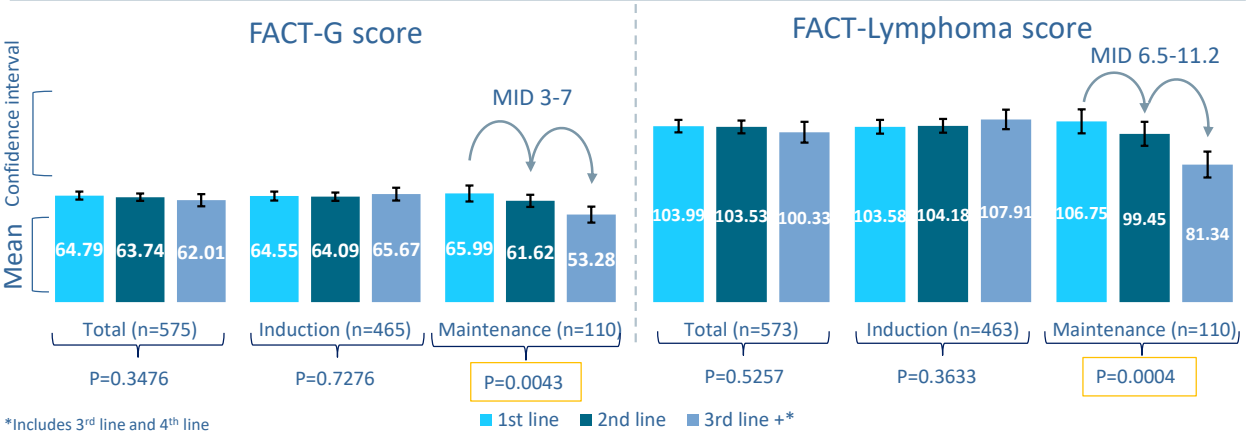
12

As for EQ5D, FACT-G and FACT-Lymphoma confirm worse outcomes for later line maintenance patients

Weighted means between patient line of therapy and FACT-G and FACT-Lymphoma scores
Significant difference between lines, n=575



*Includes 3rd line and 4th line

Note: FACT-LymS score ranges from 0-60, FACT Lymphoma TOI scores range from 0-116, FACT-G score ranges from 0-108 and FACT Lymphoma score ranges from 0-168. The higher the score, the better the QoL.

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13

Conclusions

- Presence of **comorbidities, ECOG score and line of therapy** are all **key predictors in an FL patient's QoL**
  - Age and presence of bulky disease were not predictors of QoL
  - No significant association between type of treatment and QoL outcomes were observed
- Patients on **maintenance therapy in later lines show a significant decrease in QoL**, highlighting the need for novel options to maintain QoL in relapsed and maintenance settings

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14

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BACKUP

Methods

- Data were drawn from the 2017 Adelphi Real World Disease Specific ProgrammeTM (DSP) in FL conducted in France, Germany, Italy, Spain and the UK (EU5) between May and July 2017. The DSP methodology has been published and validated previously.
- The FL DSP is a point-in-time study administered to haemato-oncologists who completed physician-reported record forms for their next 8 consulting patients with FL with whom they consulted. Patients were then asked to complete self-completion forms (PSC), participation was voluntarily.
- Data collection included patient demographics, background clinical information and treatment patterns, including line and type of treatment from the patient-record form (PRF), and PRO tools measuring QoL including FACT, WPAI and EQ5D.
- Patient inclusion criteria for this analysis were age ≥18 years, a physician-confirmed diagnosis of FL, not currently enrolled in a clinical trial and receiving an active drug treatment (either induction or maintenance).
- Statistical methods included Spearman's rank correlation co-efficient, bivariate tests including; Mann-Whitney test (MW), Kruskal-Wallis test (KW), Fisher's Exact (FE), Pearson's Chi-Squared (PC), Student's T-test (TT), ANOVA (AN) and Pearson's Chi-Squared test (CH), and a multiple linear regression.
- Minimal important differences (MID) ranged from 2.9-5.4 for FACT-lymphoma subscale, 5.5-11 for FACT lymphoma TOI, 6.5-11.2 for FACT-Lym score [3], 2-3 for FACT-PWB, 2 for FACT-EWB, 2-3 for FACT-FWB, and 3-7 for FACT-G scores[4]. For the EQ5D utility score the MID is 0.10.

Methods – Minimum important differences

PRO Tool	MID
FACT-Lymphoma Subscale	2.9-5.4
FACT-Lymphoma TOI	5.5-11
FACT-Lym score	6.5-11.2
FACT-PWB	2-3
FACT-EWB	2
FACT-FWB	2-3
FACT-G	3-7
EQ-5D Utility score	0.10

References:
- Webster K, Cella D and Yost K. (2003). The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. *Health Quality of Life Outcomes*. 1 (79)
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Results – Demographics (PSC vs Non-PSC)

- Data analysis was conducted on 1,520 patients diagnosed with FL, of whom 585 completed a PSC.
- Patients that completed a PSC were more likely to be at 1st line (31% vs 23%; p=0.0009), responding to treatment at time of study (22% vs 16%; p=0.0060) [table 1] and experience fewer comorbidities (1.2 vs 1.3; p=0.0338) than those that didn't complete a PSC.
- Highest PSC completion rates were seen in France (39%), Germany (29%) and Spain (15%). Italy and UK showed the lowest rates of completion (14%; 4%).
- Characteristics of patients that completed a PSC were: mean age 65.1 years (SD=11.3), patients were most commonly grade 2 and stage III (43%; 41%), on their 2nd line of therapy (59%) and had an ECOG of 1 (53%) [table 1].
- Patients that completed a PSC were more likely to be received R-CHOP (24% vs 17%; p=0.0015) at time of data collection than patients that didn't complete a PSC, this however varied by line of therapy [figure 1].

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Table 2: QoL scores dependent on EQ5D utility score

	Spearman's rank correlation coefficient score	Prob > |t| (if <0.05, EQ5D (5L) and QoL score are assumed to be independent)
WPAI activity impairment	-0.5639	0.0000
FACT-Lymphoma TOI score	0.7417	0.0000
FACT-G score	0.6729	0.0000
FACT-Lymphoma score	0.7323	0.0000

	Spearman's rank correlation coefficient score			Prob > |t| (if <0.05, EQ5D (5L) and QoL score are independent)		
	1st line	2nd line	3rd line or later*	1st line	2nd line	3rd line or later*
ECOG score	-0.1713	-0.4396	-0.6881	0.0215	0.0000	0.0000
Comorbidities	-0.2391	-0.3196	-0.4566	0.0012	0.0000	0.0001

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Further results

- Patients on later lines of therapy had worse QoL (line 1-line 3+; p-value), including EQ5D-5L (0.82-0.60; p<0.0001), FACT-G score (67.79-55.88; p<0.0001), and FACT-Lymphoma score (109.29-89.63; p<0.0001).
- With increasing lines of therapy, patients receiving induction therapy had better QoL compared to those on maintenance therapy. For patients on induction therapy, EQ5D-5L decreased from 0.81 to 0.78 (p=0.4193), FACT-G score decreased from 66.42 to 64.03 (p=0.1615), and FACT-Lymphoma score decreased from 106.86 to 105.05 (p=0.3000) from 1st line to 3rd line +.
- For patients on maintenance therapy, EQ5D-5L decreased from 0.86 to 0.23 (p=<0.0001) FACT-G decreased from 72.05 to 38.77 (p=<0.0001), and FACT-Lymphoma score decreased from 116.80 to 57.23 (p=<0.0001) from 1st line to 3rd line+.
- **EQ5D-5L, FACT-PWB, FACT-FWB, FACT-EWB show MID from 1st to 3rd (and 4th) line for patients on maintenance.**
- **FACT Lymphoma TOI, FACT-G and FACT-Lymphoma scores all show MID from 1st to 2nd line and 2nd to 3rd (and 4th) line for patients on maintenance.**

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