Therapeutic monitoring of TNF-alpha inhibitors in rheumatoid arthritis [DAR17/10/02]

Addendum #3

Sensitivity analysis:

Arango (2017) remission and LDA/active disease:

Adalimumab and Promonitor

7 February 2019

This addendum was produced in response to a stakeholder comment. The results from the abstract of the INGEBIO trial published by Arango and colleagues (2017) provided the number of days in remission or LDA. Using these data led to substantial differences in model results compared to using the data from the same (INGEBIO) trial published by Ucar and colleagues (2017).

The manufacturer provided data on the number of days in remission during the follow-up period for the data cut from the INGEBIO trial reported in Arango and colleagues (2017); i.e intervention group follow-up of 530.8 days and control follow-up 544.6 days (Table 1).

Table 1: Total number of days in remission during follow-up period (Arango and colleagues 2017: Scenario 2 remission and LDA/active disease)

Group	Mean	N	SD	Sum	Median
Control	360.00	52	226.181	18720	401.00
Intervention	362.22	98	213.997	35498	437.50
Total	361.45	150	217.542	54218	431.00

Key: LDA low disease activity; SD = standard deviation

A scenario analysis was conducted using these data and applying the relevant utility values and management of health state costs for the remission and LDA/active disease health states.

Adalimumab and Promonitor: threshold analysis

The results of the threshold analysis are presented in Table 2. Results based on the longer-term follow-up (Arango and colleagues, 2017) suggested that monitoring is more costly and produces slightly fewer QALYs than standard care.

Figure 1 shows the annual cost of ELISA-based testing at which TDM would become cost-effective at the two WTP thresholds used in NICE decision making for the range of ADL acquisition costs of £1,000–£9,187.

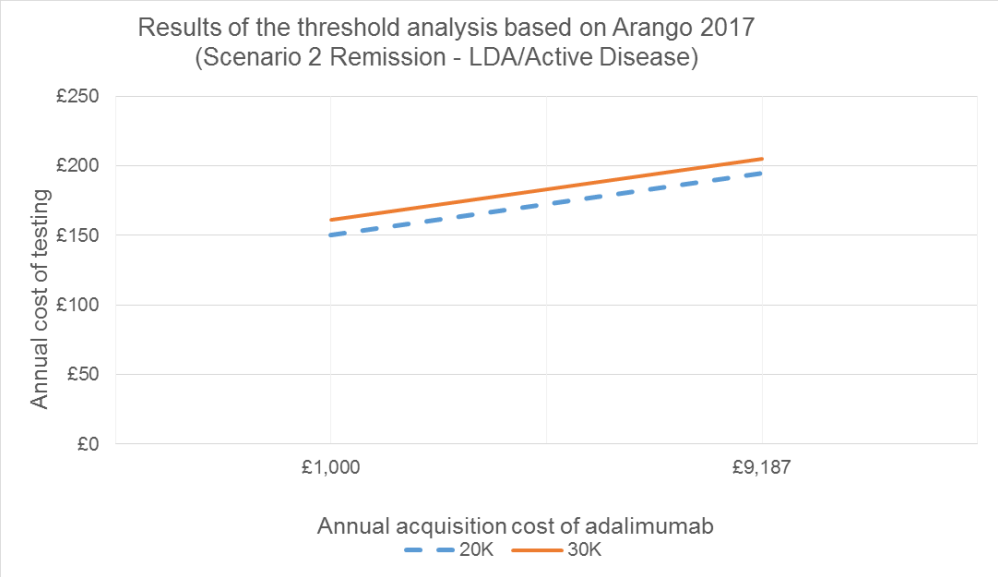
Using the data from Arango and colleagues (2017) (mean duration in remission), with the current price of originator ADL, testing would need to be cheaper than £194 per year in order for TDM to be judged as cost-effective at the cost-effectiveness threshold of £20,000 per QALY gained.

Table 2: Threshold value for the cost of testing at which NMB is zero

ICER threshold	Results based on INGEBIO study, Arango and colleagues 2017 (Scenario 2: remission and LDA/active disease)	
	£1,000	£9,187
20K	£150	£194
30K	£161	£205

Key: ICER: incremental cost-effectiveness ratio; LDA = low disease activity; NMB, net monetary benefit

Figure 1: Results of the threshold analyses using Arango and colleagues (2017) (Scenario 2: remission and LDA/active disease)



Key: LDA = low disease activity

Adalimumab and Promonitor: cost utility analysis

The incremental QALYs and incremental costs for testing versus standard care strategy are shown in Table 3.

Table 3: Cost-effectiveness results in patients in remission and LDA/active disease treated with Humira® and tested using Promonitor

	Intervention	Control	Differential
Drug acquisition	£13,075	£13,149	-£74
Drug admin	£0	£0	£0
Drug wastage	£527	£530	-£3
Cost of managing health states	£22,371	£22,436	-£65
Cost of flare management	£303	£418	-£115
Cost of managing AEs	£69	£70	£0
Cost of phlebotomy appointment	£162	£0	£162
Other costs of testing	£30	£0	£30
Cost of sample transport	£6	£0	£6

	Intervention	Control	Differential
Total costs:	**£36,543**	**£36,602**	**-£59**
QALYs			
Remission	0.712	0.708	0.004
LDA/active disease	0.284	0.287	-0.003
Flares	-0.002	-0.003	0.001
AEs	-0.001	-0.001	0.000
Total QALYs	**0.993**	**0.992**	**0.002**
ICER			**-£36,717**

Key: AEs = adverse events; ICER = incremental cost effectiveness ratio; LDA = low disease activity; QALYs = quality adjusted life years

Summary

In the primary analysis, using data from Arango and colleagues (2017), TDM was dominated (remission/LDA and active disease scenario); however, using the data provided (remission and LDA/active disease) the results of the analysis were in the same direction as results from the analysis using Ucar and colleagues (2017); i.e. therapeutic drug monitoring (TDM) is expected to be less costly with slightly more quality-adjusted life years (QALYs) than standard care.

In both the threshold and the cost-utility analyses for Arango and colleagues (2017) (remission and LDA/active disease [Scenario 2]), however, the cost-effectiveness of TDM of TNF-alpha inhibitors in RA remains considerably uncertain. The results are based on very small and uncertain differences in outcomes (QALY differences of less than 0.01). It is also not possible to argue that either the analysis based on Ucar and colleagues (2017) or that based on Arango and colleagues (2017) is more valid than the other – they both have significant weaknesses (refer to Section 2 of the main report). The follow-up in Arango and colleagues (2017) is over a longer time horizon (545 days in the control arm) than Ucar and colleagues (2017) (505 days in the control arm). A conservative assumption is applied in the model in that the same follow-up period is applied for both the intervention and control arms. The number of days in the LDA/active disease health state is calculated by subtracting the number of days spent in remission from the total length of follow-up (i.e. the intervention group were assumed to spend 13.8 days in the LDA/active disease state). Thus there is uncertainty around the progression of participants in the intervention group after 531 days.