European Crohn's and Colitis Organisation

Anti-TNF Re-Induction is as effective, simpler and cheaper compared with Dose Interval Shortening for secondary loss of response in Crohn's disease:

A 'real world' study

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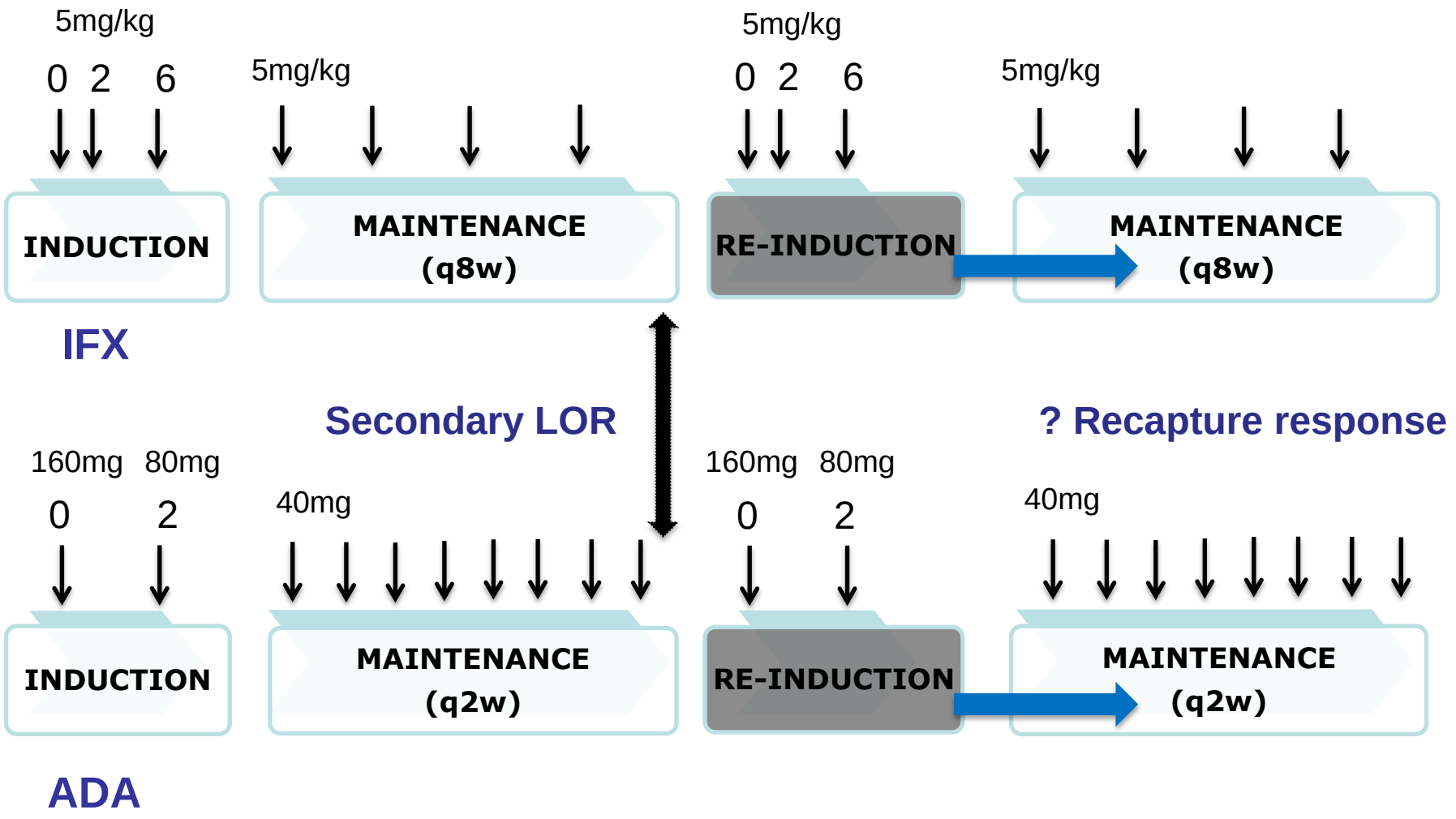
Disclosure of Conflicts of Interest:

Conflict of interest : NONE

Background

- Secondary loss of response (LOR) occurs in up to 60% of patients treated with infliximab (IFX) or adalimumab (ADA)
  (Ma et al. Journal Clinical Gastro. 2015)
- Therapeutic options for secondary LOR include
  1. Re-induction (RI) with current anti-TNF
  2. Switching anti-TNF and/or consideration of another agent
  3. Dose intensification
     a. Dose interval shortening (DIS)
     b. Dose increase with same interval
- DIS is expensive, tendency to continue long-term, ***BUT***
  - LOR may be transient *(Gisbert et al. American Journal of Gastro, 2009)*
  - RI offers transient dose intensification, preventing 'set and forget' mentality…

What is RE-INDUCTION?



Aims & Methods

Retrospective observational study (Jan 2006 – Aug 2016)

1. Evaluate the 'real world' efficacy of RI and/or DIS following secondary LOR to maintenance anti-TNF in Crohn's disease
2. Determine factors associated with durability of response following RI and/or DIS
3. Compare the relative costs of RI versus DIS

**DIS refers to 6-weekly IFX (5mg/kg) or weekly ADA (40mg)*

Results – pre-RI/DIS

Pre RI and DIS	RI n= (%)		DIS n= (%)		p-value
No of patients	33	(38)	55	(63)	
Females	17	(52)	25	(45)	0.66
Smoker (incl ex-smoker)	16	(48)	10	(18)	**< 0.01**
Prior Surgery	14	(42)	26	(47)	0.83
Complicated Disease	29	(88)	51	(93)	0.47
Prior aTNF Exposure	9	(27)	21	(38)	0.36
Infliximab	22	(67)	29	(53)	0.27
Co-therapy	25	(76)	49	(89)	0.13
Subtherapeutic aTNF drug levels (IFX < 3, ADA < 5)	8	(24)	43	(78)	**< 0.01**
Median Age at RI/DIS (years)	35.03		37.00		1.00
Median Disease Duration at RI/DIS (years)	8.15		10.23		NS
Median time to secondary LOR (years)	1.84		2.47		0.79

Results – post RI/DIS

	RI n= (%)		DIS n= (%)		p-value
Post RI and/or DIS					
Median time to treatment failure (years)	0.98		0.77		0.34
Treatment failure < 12 months	8	(24)	8	(15)	0.27
Treatment failure < 24 months	10	(30)	11	(20)	0.31
Required Surgery prior to change in aTNF	4	(12)	0	(0)	**0.02**
Median follow up post RI/DIS (years)	3.45		1.53		

Treatment failure was defined as:

The occurrence of surgery, change or cessation of anti-TNF following RI or DIS

Multivariate linear regression analysis:
Factors associated with longer time to treatment failure post RI or DIS

↑ Time to failure

- **Higher baseline Albumin** (p<0.01)
- **Male sex** (p=0.03)
- **Thiopurine co-therapy** (p=0.04)
- **IFX rather than ADA used** *(p=0.06)*

↓ Time to failure

- **Higher baseline calprotectin** (p=0.03)

Non significant associations:

- Smoking status (p=0.68)
- Serum CRP (p=0.46)
- Duration on same anti-TNF prior to RI or DIS (p=0.45)

**Presented in decreasing magnitude of effect size (ie standardised B coefficient) within model*

Real world cost analysis in this cohort

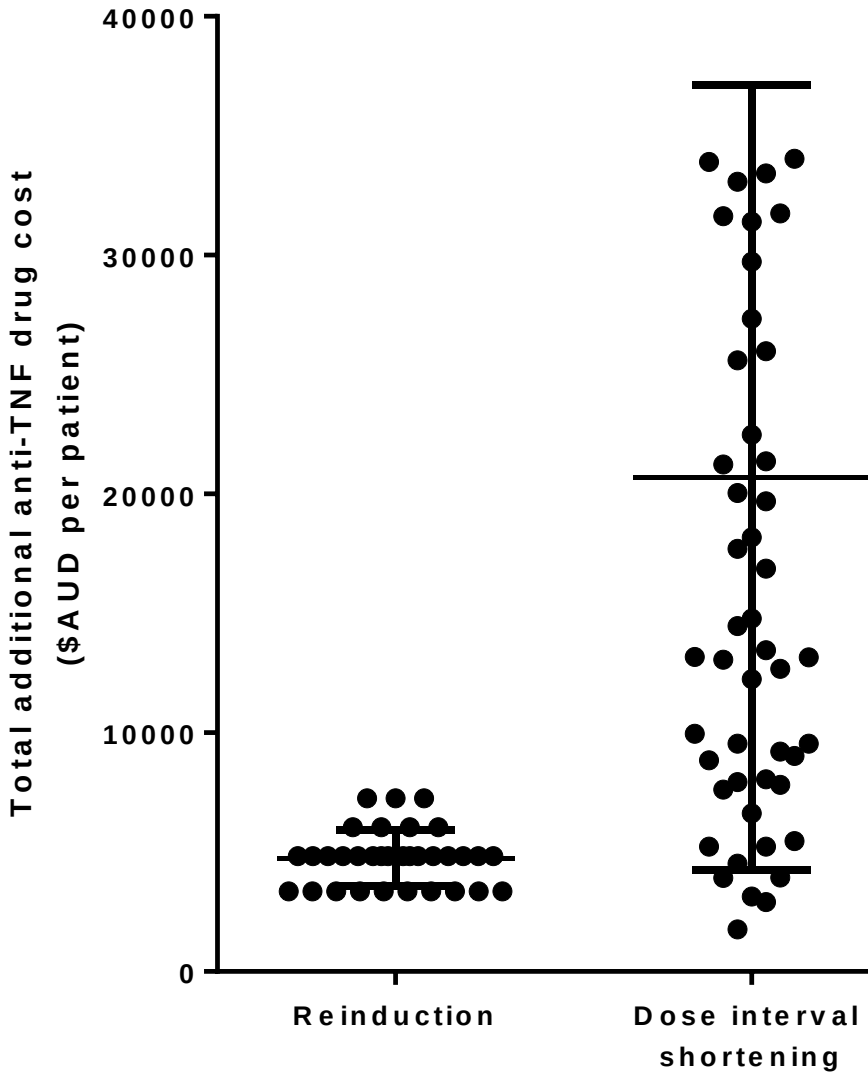
	RI	DIS	p value*
Median additional anti-TNF drug cost *($AUD)*	**4 839**	**13 190**	<0.01
Median extra doses as per 'real world' cohort *(vs standard dosing in same period)*	**2.0**	**7.0**	<0.01

Based on

- Actual number of doses received
- Australian PBS wholesale drug costs as of 31/5/2016
- Duration of anti-TNF RI or DIS therapy to failure / follow-up

**Mann Whitney tests*

**RI is significantly cheaper than DIS*



Conclusions

- Our 'real world' data suggest that:
  - Applying RI first-line was of ***comparable efficacy*** and significantly ***less expensive*** compared to DIS

Future directions

Should we apply RI prior to DIS…..?

- Prospective studies comparing relative efficacy of RI and DIS are needed
- Evidence based guidelines are required to inform de-escalation following DIS to ensure **$**ustainability

A proposed approach to anti-TNF re-induction

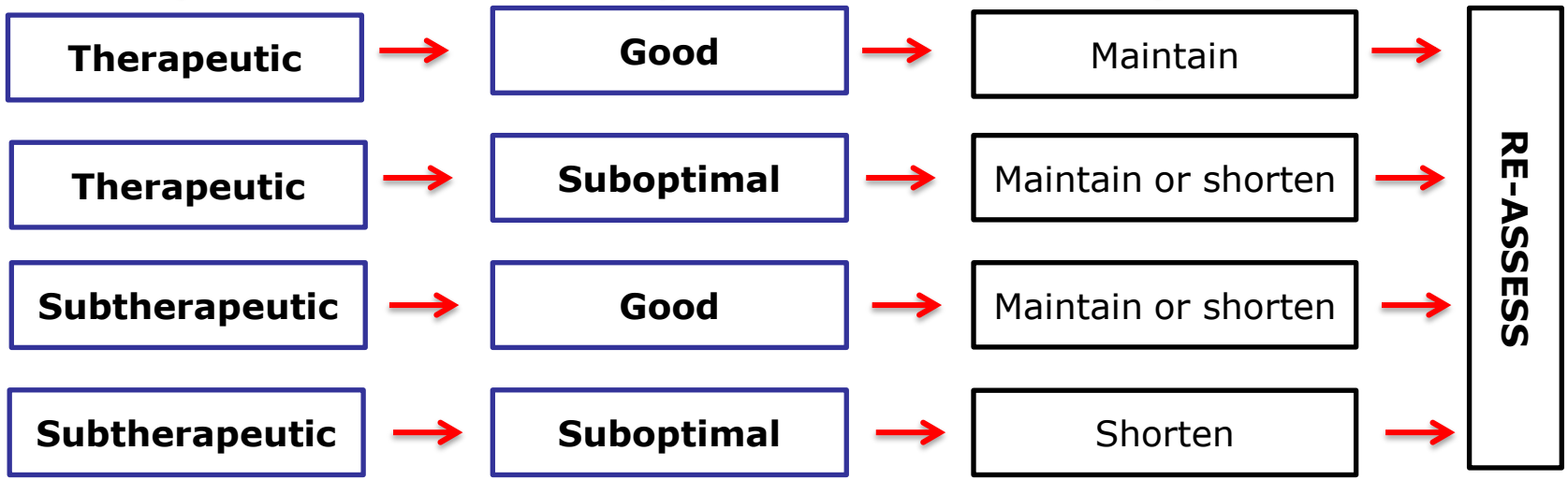
1. Secondary LOR **WITH** Low [anti-TNF] trough

2. 1st line RE-INDUCTION

3. Re-assess [anti-TNF] trough

4. Re-assess clinical response

5. Manage interval



THANK YOU