Infliximab drug survival in chronic plaque psoriasis: follow up of the product familiarisation program

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Abbreviations: CPP, chronic plaque psoriasis; PFP, product familiarisation program; TNF, tumour necrosis factor; PASI, psoriasis area and severity index; DLQI, dermatology quality of life index; SCC, squamous cell carcinoma

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Introduction

Here we present an updated case series of 22 patients with chronic plaque psoriasis (CPP) from the product familiarisation program (PFP), that took place in 2007 prior to the listing of infliximab on the Pharmaceutical Benefits Scheme in December 2007^[1].

Infliximab is a chimeric monoclonal antibody against tumour necrosis factor (TNF)- α administered by intravenous infusion. In randomised controlled trials, 80% of patients achieve a 75% reduction in psoriasis area and severity index (PASI75) from baseline at 10 weeks, and 61% of patients sustain PASI75 at 50 weeks^[2, 3].

Main text

All patients enrolled in the PFP met the eligibility criteria of being at least 18-years old, having moderate to severe CPP for more than 6 months and a PASI of more than 15. In addition, patients had to have demonstrated inadequate response or intolerance to three of four treatment strategies: phototherapy (minimum three treatments per week), methotrexate (minimum 10mg weekly), ciclosporin (minimum 2mg/kg daily), and acitretin (minimum 0.4mg/kg daily). Exclusion criteria included pregnancy, severe infection,

congestive heart failure, malignancy, and hypersensitivity to infliximab or other murine proteins.

Infliximab was administered by intravenous infusion at 5mg/kg at weeks 0, 2, and 6 for induction and 8 weekly thereafter for maintenance. During each clinical visit PASI and dermatology quality of life index (DLQI) were recorded.

The previous report included data up to 2012^[1]; at that time seven of the original 22 patients remained on treatment with infliximab (Table 1). Of these, four continued on infliximab at the end of the current study (Cases 4, 5, 6, 16) and one patient had a break from infliximab for overseas travel, recommencing therapy upon return (Case 19). Overall, this indicates a sustained response in these patients (Figure 1). All patients who continued infliximab beyond the original study period achieved PASI75, four PASI90, and three PASI95 (Table 2).

For those patients who ceased since the previous study: one patient ceased voluntarily after over 11 years of treatment, citing difficulty attending infusions (Case 18, PASI at cessation 0.6, 98% reduction from baseline); one patient ceased after ten years of treatment, due to numerous squamous cell carcinomas (SCC, Case 22, PASI at cessation 1.5, 93% reduction), and one patient experienced loss of efficacy (Case 11, PASI at cessation 5.6, 79% reduction).

From the original 22 patients enrolled in the PFP^[1], four patients developed a serious adverse event, and four were lost to follow-up (Table 1). As reported previously, one patient developed invasive SCC of the nose. Two patients died during the initial study period. One passed away from multiorgan failure; factors thought to have contributed to the death were excessive alcohol consumption and the patient supplementing his biologic therapy with ciclosporin and methotrexate between infusions. The other patient had a fall the day prior to his death on anti-coagulation, the patient was found unresponsive the following day. In both cases no autopsy was performed. In 2012 one patient developed a melanoma after stopping infliximab in 2008. This was treated with wide-local excision, and the patient has continued on ustekinumab without recurrence. Otherwise there were no new serious adverse events from the time of the previous

study. Minor adverse events included deranged liver enzymes, non-melanoma skin cancers and non-serious infections these did not alter infliximab treatment. The patients with liver dysfunction did not have cirrhosis, and was thought to be a combination of treatment with infliximab and methotrexate, alcohol consumption, and obesity. In discussion with a hepatologist, methotrexate was weaned from 20mg to 10mg weekly and eventually ceased. The patient was able to reduce his alcohol intake and reduce weight, and his liver enzymes have subsequently improved; he remains on infliximab monotherapy.

The four patients lost to follow-up included two patients who moved overseas, at that time PASI were 8.4 (52% reduction) and 7.6 (83.5% reduction) respectively. The remaining two patients included one patient who ceased voluntarily, at cessation PASI score was 14 (76% reduction), and one patient who did not continue attending the clinic, at the time of transfer the PASI was 2.3 (90% reduction).

Conclusion

Although small, this series adds to the existing safety data for infliximab and demonstrates sustained response to treatment^[4-6]. In this cohort, five of 22 patients continued infliximab more than a decade after commencing. Importantly all patients treated with infliximab beyond the period of the original study experienced sustained response to treatment and there were no further serious adverse events in those continuing infliximab.

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Case	Sex	Age	Age at onset	Baseline PASI	Outcome	Adverse event
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Figure 1

Figure legends

Figure 1. Kaplan-Meier curve demonstrating percentage of patients remaining on infliximab over time

Tables

Table 1. Patient characteristics and outcomes on infliximab. Abbreviations: PASI, psoriasis area severity index; DLQI, dermatology quality of life index; SCC, squamous cell carcinoma; BCC, basal cell carcinoma; UTI, urinary tract infection; URTI, upper-respiratory tract infection.

1	F	52	20	25.4	Infliximab Nov 2006 - Feb 2007 Methotrexate commenced 2006, dose 10mg	Lost to follow up
2	M	71	55	17.6	Infliximab Dec 2006 - Oct 2011	Death 2011
3	F	43	6	18.6	Infliximab May 2007 - Nov 2007 Methotrexate commenced Dec 2006. dose 10mg	Moved overseas, lost to follow up
4	M	65	27	26.5	Infliximab Feb 2007 - unknown Methotrexate commenced Sep 2009, dose 5mg	Lost to follow up
5	M	64	26	27.7	Infliximab Nov 2006 - current	
6	M	66	33	31.1	Infliximab Mar 2007 - current Methotrexate commenced May 2008, dose 20mg	Liver enzyme derangement UTI 2011 BCC 2013 Pneumonia 2014 SCC 2015
7	F	57	14	15.4	Infliximab Apr 2007 - Mar 2010 Etanercept Mar 2010 - current Methotrexate commenced Oct 2009, dose 10mg	
8	M	43	10	46.2	Infliximab Mar 2007 - Nov 2009 Ustekinumab Oct 2009 - July 2010 Adalimumab July 2010 - Sept 2014 Ustekinumab Mar 2014 - May 2014 Methotrexate commenced in Feb 2009, dose 20mg	Moved overseas, lost to follow up
9	M	68	28	58.8	Infliximab Apr 2007 - Nov 2009 Ceased biologics voluntarily (changed to natural remedies)	Lost to follow up
10	M	50	30	16.2	Infliximab May 2007 - Apr 2010 Ceased biologics voluntarily	
11	M	68	40	26.8	Infliximab Jan 2006 - August 2011 Ustekinumab Aug 2011 - current	
12	M	48	19	39.6	Infliximab May 2007 - Oct 2008 Adalimumab Nov 2008 - Oct 2009 Ustekinumab Oct 2009 – current	Shingles 2011 Dental abscess 2013
13	M	60	12	21.4	Infliximab May 2007 - Apr 2008 Adalimumab Apr 2008 - Oct 2009 Ustekinumab Oct 2009 - current Methotrexate commenced Jan 2010, dose 10mg.	Melanoma 2012

14	M	65	33	18.1	Infliximab May 2007 - Aug 2008	Death 2008
15	F	65	43	27.2	Infliximab May 2007 - Oct 2009 Fumaric acid esters May 2010 - Aug 2014 Ustekinumab Aug 2014 - current	Invasive SCC on nose 2009 BCC 2015 BCC 2016 BCC 2016 SCC in situ 2017
16	M	76	31	25.2	Infliximab Jul 2007 - current Acitretin Nov 2011 - current (10mg)	
17	M	57	30	39	Infliximab May 2007 - Oct 2009 Ustekinumab Oct 2009 - Dec 2009 Adalimumab Jan 2010 - Jun 2018 Ixekizumab Jun 2018 – current	URTI 2011 URTI 2011 Dental abscess 2013 SCC 2019
18	M	53	21	32.2	Infliximab June 2007 - Mar 2019 Tildrakizumab Jul 2019 – current	
19	M	33	1	25.4	Infliximab May 2007 - Jul 2012 Recommenced Nov 2012 – current	Tinea pedis 2018
20	M	72	40	20.9	Infliximab Jul 2007 - Jul 2010 Adalimumab Jul 2010 – current	UTI 2011
21	M	49	7	16.1	Infliximab Jul 2007 - Jun 2009 Adalimumab Jul 2009 – current	
22	M	72	40	21.9	Infliximab Aug 2007 - Oct 2017 Ustekinumab Nov 2017 – current	Multiple SCC 2009 - 2018

Table 2, PASI improvement from baseline for cases continuing infliximab beyond the period of the original case series. * Denotes current treatment with infliximab

Case	Baseline PASI	PASI at infliximab cessation	Duration of treatment with infliximab (months)
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4	26.5	1.2	157 *
5	27.7	3.8	160 *
6	31.1	3.8	156 *
11	26.8	5.6	67
16	25.2	2.1	160 *
18	32.2	4.6	141
19	25.4	0	159 *
22	21.9	0.2	122

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