

The effects of EBV naïve status on treatment decisions in patients with Inflammatory Bowel Disease: Does the risk of GI lymphoma justify the cost?

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Background

Whilst thiopurines and biologics have revolutionised the treatment of Inflammatory Bowel Disease (IBD), there has been worldwide recognition of the risk they confer of subsequent lymphoma development, particularly with thiopurine use, through their association with Epstein Barr Virus (EBV).

The resulting lymphomas have shown to bare histological resemblance to post-transplant lymphoproliferative disorders (PTLD) and research in both PTLD and IBD has revealed that whilst latent infection with EBV carries a risk of seroconversion, it is EBV naïve individuals who appear to be most at risk.

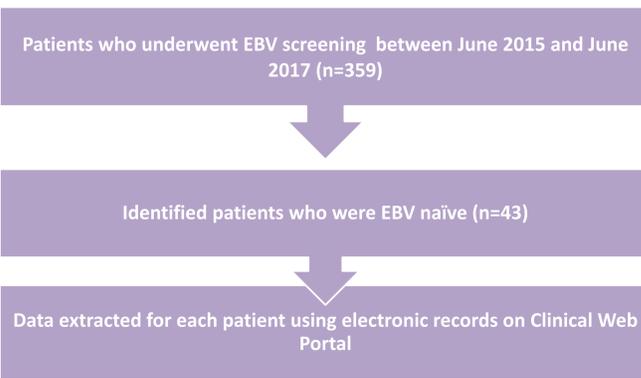
This forms the basis of guidance produced by the European Crohn's and Colitis Organisation (ECCO) who recommend testing EBV status prior to initiating immunomodulator therapy.

This audit identifies treatment decisions made in EBV naïve patients and the subsequent cost expenditure.

Objectives

- To identify the effects of EBV naïve status on treatment decisions, in particular looking at whether EBV naïve status leads to Biologic therapy in those initially considered for thiopurine therapy.
- To calculate the financial cost as a result of the treatment decisions made due EBV naïve status.
- To evaluate the clinical need of using EBV status when initiating treatment in IBD patients.

Methods



Results

Sample demographics

- The sample of patients who underwent EBV screening in the specified time period consisted of 206 males (57%) and 153 females (43%).
- Overall median age was 46.1 years.
- 316 (88%) patients were EBV positive and 43 (12%) were EBV naïve.
- Of the 43 EBV naïve patients 9 patients were excluded from further analysis.

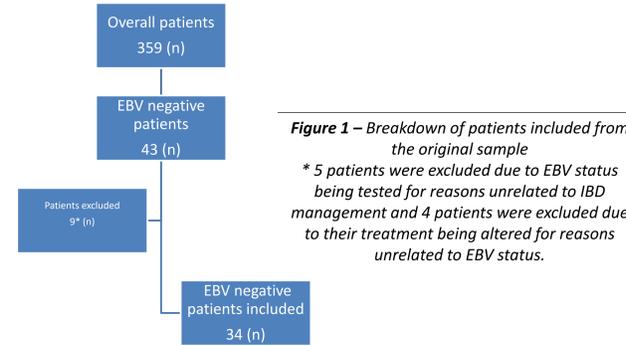


Figure 1 – Breakdown of patients included from the original sample
* 5 patients were excluded due to EBV status being tested for reasons unrelated to IBD management and 4 patients were excluded due to their treatment being altered for reasons unrelated to EBV status.

Patient Demographics: EBV positive vs. EBV naïve

EBV Positive N (%)	EBV Naïve N (%)
Caucasian 236 (75)	Caucasian 34 (79)
Indian 41 (13)	Indian 7 (16)
Other 25 (8)	Other 1 (2)
Not recorded 13 (4)	Not recorded 1 (2)

Figure 2 – Patient ethnicity in EBV positive patients compared with EBV naïve patients n (%)

% Age distribution in EBV Positive patients

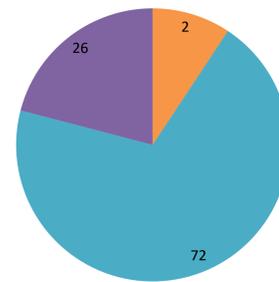


Figure 3 – Percentage of patients aged < or equal to 18, between 19-60 and >60 who were EBV positive

% Age distribution in EBV Naïve patients

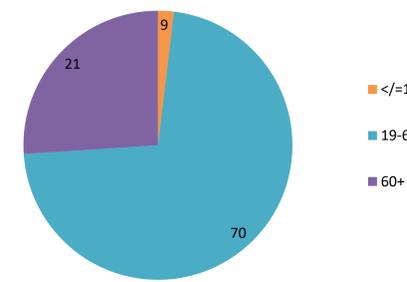


Figure 4 – Percentage of patients aged < or equal to 18, between 19-60 and >60 who were EBV naïve

- There was no differences in patient ethnicity or age between the EBV positive and EBV naïve group.
- Mean age in the EBV positive group was 47.1 and in the EBV naïve group was 40.1.

Treatment decisions in EBV naïve patients

- Overall, of the EBV naïve patients, 18 (42%) had a diagnosis of ulcerative colitis and 25 (58%) had a diagnosis of Crohn's disease.
- Of the 34 EBV naïve patients included, 22 (65%) underwent EBV screening as part of the pre-screening for thiopurine use of which 2 were screened for Mercaptopurine and 20 were screened for Azathioprine, 6 (18%) were screened prior to initiating biologic therapy, 1 (3%) patient was screened prior to initiating combination therapy and 5 (15%) patients underwent EBV screening as part of general pre-screening bloods.

Table 1 – Number of patients undergoing EBV screening for initial thiopurine or biologic therapy and the resulting number of patients in whom therapy was switched and the subsequent cost expenditure on average per patient. *Calculated based on the cost of 12 months of treatment in a 70kg individual **Patients underwent EBV screening as part of generic pre-screening bloods

No of patients screened (n)	Initial treatment agent considered	No of patients in whom treatment was altered (n)	Agent changed to	Average increased cost expenditure per patient
22	Thiopurine	12	Biologic	£9942*
6	Biologic	-	-	-
5	**	1	Biologic	£4112*
1	Combination therapy	-	-	-

Table 2 – Characteristics of patients in whom treatment was switched

Demographic	Gender		Ethnicity	
	Male	Female	Caucasian	Indian
No. of patient n (%)	8 (62)	5 (38)	10 (77)	3 (23)

- Of the 20 patients tested prior to Azathioprine treatment, 12 (60%) patients had their treatment switched to a biologic due to EBV naïve status, of which 11 (92%) were started on Adalimumab. Switching therapies resulted in an average increase in cost expenditure of £9942 per patient. 5 (25%) patients did not require treatment escalation and 3 commenced Azathioprine despite their EBV naïve status.
- All patients who were screened for Mercaptopurine therapy, combination and biologic therapy commenced treatment.
- Of the 5 who underwent general pre-screening bloods, 4 patients remained on 5-ASA treatment whilst 1 commenced biologic treatment due to their EBV naïve status.
- Of the 13 individuals who had their therapy switched 8 (62%) were male and 10 (77%) were Caucasian.

Financial Breakdown of Switching Treatment

All patients who had their therapies switched were or would have been considered for Azathioprine initially.

No of patients	Cost of Initial treatment agent considered/yr (£)	Agent switched to	Cost of therapy switched to /yr (£)	Therapy cost difference (£)
11	1,103	Adalimumab	116,295	115,192
1	100	Infliximab	4,212	4,112
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The total cost of switching patients from Azathioprine to other biologic therapy was approximately £123,416.

Discussion

- Overall 38% (13) patients were commenced on a different treatment as a result of the EBV naïve status.
- This led to a cost expenditure of approximately £123,000 per year.
- However, as the absolute risk of lymphoma remains low and given the increased likelihood of patients without pre-treatment with AZA subsequently developing antibodies to biologic agents, is this increase in cost expenditure truly justified?

Figure 5 – A breakdown of patients showing initial treatment agent considered and treatment commenced in those who had their therapies switched due to EBV naïve status.

