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

The Royal Wolverhampton NHS Trust, Wolverhampton, United Kingdom

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 at most risk.

This forms the basis of guidance produced by the European Crohn’s and Colitis Organisation (ECCO) who recommend thiopurine use, through their association with Epstein Barr Virus (EBV).

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

- Patients who underwent EBV screening between June 2015 and June 2017 (n=359).
- Identified patients who were EBV naïve (n=43).
- Data extracted for each patient using electronic records on Clinical Web Portal.

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.

Patient Demographics: EBV positive vs. EBV naïve

- Overall, of the EBV naïve patients, 18 (42%) had a diagnosis of ulcerative colitis and 25 (58%) had a diagnosis of Crohn’s disease.
- 316 (88%) patients were EBV positive and 43 (12%) were EBV naïve.
- Overall median age was 46.1 years.
- 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 EBV naïve.
- There was no difference in patients 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.

Table 1 – Breakdown of patients included from the original sample

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Cost of Initial treatment agent considered/yr (£)</th>
<th>Agent switched to</th>
<th>Cost of therapy switched to/yr (£)</th>
<th>Therapy cost difference (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Adalimumab 113,295</td>
<td>Infliximab 4,122</td>
<td>111,173</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Infliximab 4,122</td>
<td>Infliximab 4,122</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

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?

Table 2 – Characteristics of patients in whom treatment was switched

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Male</th>
<th>Female</th>
<th>Caucasian</th>
<th>Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patient n (%)</td>
<td>8 (62)</td>
<td>5 (38)</td>
<td>10 (77)</td>
<td>3 (23)</td>
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</table>

- 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 biologics, 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.

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References

- Identified patients who were EBV naïve (n=43)
- Overall patients (n=348) were EBV positive.
- Overall median age was 46.1 years.
- 136 (38%) patients were EBV negative and 212 (59%) were EBV positive.
- Overall median age was 46.1 years.
- 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 EBV naïve.
- There was no difference in patients 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.

Table 2 – 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 per patient.

<table>
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<tr>
<th>No of patients screened (n)</th>
<th>Initial treatment agent considered</th>
<th>No of patients in whom treatment was altered (n)</th>
<th>Agent changed to</th>
<th>increased cost expenditure per patient (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>Thiopurine 12</td>
<td>6</td>
<td>Biologic</td>
<td>£9942*</td>
</tr>
<tr>
<td>5</td>
<td>Biologic 1</td>
<td>1</td>
<td>Combination therapy</td>
<td>£4112*</td>
</tr>
</tbody>
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