ABX464 is safe and efficacious in a proof of concept study in Ulcerative Colitis patients


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Disclosures

GSK shareholder
ABIVAX employee and shareholder options
Background

Despite the availability of new drugs, there is still a high unmet medical need for patients suffering from Ulcerative Colitis and Crohn’s Disease

ABX464

• Is a small molecule administered as an oral capsule
• Has antiretroviral properties, reduces total HIV-DNA and was studied in more than 180 subjects in HIV program (1,2)
• Has potent anti-inflammatory properties impacting the expression of miR-124 (3,4)

1 Steens et al, Antimicrob Agents Chemother 61:e00545-17
2 Rutsaert et al, Journal of Virus Eradication 2018; 5: e1–e13
ABX464 - Proposed mechanism of action

NORMAL CBC FUNCTION

1. CBC binds to the majority of RNAs generated in the nucleus and recruits factors necessary for its processing.

2. CBC binds weakly to non-coding RNA carrying anti-inflammatory factor miR-124 message is not edited.

3. Message is degraded and miR-124 is not released.

ABX464 and CBC FUNCTION

1. ABX464 acts on the CBC to increase miR-124 carrying RNA binding.

2. Increased binding promotes non-miR-124 coding RNA splicing.

3. Expression of miR-124 is increased, inflammatory brake is applied.
ABX464 showed efficacy in DSS Mice Model*

**Study Design**

*Randomized, double-blind, placebo controlled, multi-national study*

- **Study Population** = Moderate to Severe Active UC patients who failed or were intolerant to immunomodulators, Anti-TNFα, vedolizumab and/or corticosteroids
  - Confirmed UC for at least 3 months with a Total Mayo Score of 6-12 with endoscopic sub-score of 2 or 3
  - Central reading of endoscopies

- **Study Endpoints**
  - Primary = Safety
  - Secondary: Mayo Score and Endoscopy, Faecal calprotectin levels, Geboes score, miRN-124 expression, microbiome, Quality of Life (SF-36) and Pharmacokinetics

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**Randomisation 2:1**

**Induction Study (ABX464-101)**
- 8 weeks of treatment
  - ABX464 – Single Dose 50mg o.d.
  - Matching Placebo

**Open Label Extension (ABX464-102)**
- 52 weeks (Ongoing)
  - ABX464 – Single Dose 50mg o.d.
Recruitment Flow

Screened (N= 46)

Randomized (N=32)

ABX464 (N= 23)

- 2 patients prematurely withdrawn
  - 1 pt due to consent withdrawal.
  - 1 pt due to AE
  1 pt who refused to perform endoscopy at Week 8

Placebo (N= 9)

Groups were well balanced in terms of baseline characteristics, disease severity and previous use of biologicals

ABX464 Evaluable patients at Week 8
N = 20

Placebo Evaluable patients at Week 8
N = 9
Good Safety Profile

- Very consistent with previous clinical studies
- No deaths, no malignancies, no opportunistic infections, no significant changes in the laboratory parameters including WBC
- No Serious Adverse Reaction, all AE’s of mild to moderate intensity

<table>
<thead>
<tr>
<th>Patients with at least one Treatment Emergent Adverse Events</th>
<th>ABX-464 (N=23)</th>
<th>Placebo (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(&gt;15%) regardless of causality</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Any Treatment-Emergent Adverse Events</td>
<td>18 (78.3%)</td>
<td>5 (55.6%)</td>
</tr>
<tr>
<td>Gastrointestinal disorders (mainly Upper Abdominal Pain)</td>
<td>8 (34.8%)</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>4 (17.4%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Nervous system disorders (mainly Headache)</td>
<td>5 (21.7%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
Efficacy data (Day 56)

<table>
<thead>
<tr>
<th></th>
<th>ABX464 (n=20/23) PP/ITT</th>
<th>Placebo (n=9/9) PP/ITT</th>
<th>p value (PP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td>35% / 30%</td>
<td>11% / 11%</td>
<td>0.16</td>
</tr>
<tr>
<td>Endoscopic Improvement</td>
<td>50% / 43%</td>
<td>11% / 11%</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Clinical response</td>
<td>70% / 61%</td>
<td>33% / 33%</td>
<td>0.06</td>
</tr>
<tr>
<td>Total Mayo Score Reduction</td>
<td>-53%</td>
<td>-27%</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Partial Mayo score Reduction</td>
<td>-62%</td>
<td>-32%</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Faecal Calprotectin decrease &gt; 50 %</td>
<td>75%</td>
<td>50%</td>
<td>na</td>
</tr>
<tr>
<td>miR-124 expression in rectal biopsies (fold increase)</td>
<td>7.69</td>
<td>1.46</td>
<td><strong>0.004</strong></td>
</tr>
</tbody>
</table>

- Clinical remission: TMS equal or lower than 2 + no sub-score >1
- Endoscopic improvement: Endoscopy sub-score 0 or 1
- Clinical response: TMS decrease of min 3 points and 30% from baseline + decrease of bleeding sub-score of min 1 point or absolute baseline of 0 or 1
Total Mayo Score Day 0- Day 56

Box Plot of Total Mayo-Score (Study ABX464-101)

Treatment: ABX464 | Placebo

N = 20 | N = 9

P-value: 0.0272

P-value reflects the comparison of change between Day 0 and Day 56 in active versus placebo treatment.
Partial Mayo Score Day 0-Day 56

Box Plot of Partial Mayo-Score (Study ABX464-101)

Treatment:  
- ABX464
- Placebo

P-value: 0.0200

N = 20
N = 9

P-value reflects the comparison of change between Day 0 and Day 56 in active versus placebo treatment.
Mayo Score Results

ABX464: Fast onset of action and clinical responses in patients who failed on biologics
Statistically significant increase in miR-124 expression

Total blood and Rectal tissue

* p value < 0.05 (Treatment and time point)
Maintenance Phase: 6 and 9-months interim analysis

• 22/23 patients including 7 patients initially on placebo enrolled in the induction phase (2 countries did not grant regulatory clearance because of lack of efficacy data at the time of submission)

• 3 patients dropped out
  • One Lack of Efficacy at M1, initially on ABX464
  • One due to subject’s decision despite clinical response at M4, initially on ABX464
  • One due to TEAE (Headache, grade 2, drug related according to PI) occurring 4 months after first dosing at M5, initially on placebo

• All other 19 patients ongoing

• As of May 20, 2019 the cumulative exposure is the following:

<table>
<thead>
<tr>
<th>Mean (Days)</th>
<th>415</th>
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<tbody>
<tr>
<td>Median (Days)</td>
<td>401</td>
</tr>
<tr>
<td>Max (Days)</td>
<td>537</td>
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<tr>
<td>Min (Days)</td>
<td>321</td>
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</table>
Maintenance Phase: 6 and 9 Months interim analysis Partial Mayo Score

Box Plot of Partial Mayo-Score (using LOCF method)  
(Study ABX464-101&102)

Treatment:  
- ABX464 - ABX464  
- Placebo - ABX464

<table>
<thead>
<tr>
<th>Time</th>
<th>N</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Day 0 (Induction)</td>
<td>13</td>
<td>ABX464 - ABX464</td>
</tr>
<tr>
<td>Month 6 (Maintenance)</td>
<td>6</td>
<td>Placebo - ABX464</td>
</tr>
<tr>
<td>Month 9 (Maintenance)</td>
<td>13</td>
<td>ABX464 - ABX464</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Placebo - ABX464</td>
</tr>
</tbody>
</table>
Maintenance Phase: 6 and 9 Months interim analysis Faecal Calprotectin

Box Plot of Fecal Calprotectin (using LOCF method)
(Study ABX464-101&102)

Treatment: ABX464 - ABX464  Placebo - ABX464

N = 13  N = 6  N = 13  N = 6

Day 0 (Induction)  Month 6 (Maintenance)  Month 9 (Maintenance)
Maintenance Phase : 9 Months interim analysis

• At 9 months, all 19 patients were still in study

• From these 19 patients, 18 patients have clinical response :
  • 7 patients (6 initially on ABX464, 1 initially on PLO) were in clinical remission at the end of the 8 weeks induction phase. After 2 months maintenance, clinical remission was confirmed in all 7 patients and they all continued to have clinical response at month 9. Endoscopy is planned at month 12.
  • 12 patients (7 initially on ABX464, 5 initially on PLO) were not in clinical remission but 6 had clinical response at the end of the 8 weeks induction phase. After 2 months maintenance, 6 patients had endoscopic improvement and 11 patients have clinical response at month 9. Endoscopy is planned at month 12.

• Calprotectine levels normalised from median 1044 µg/g at baseline to 23.5 µg/g at Month 9.
Conclusions

• New mechanism of action ORAL drug ABX464
• Promising preclinical data in IBD model
• Good Safety and tolerability of ABX464 in UC patients and HIV program in more than 200 subjects treated (No Serious Adverse Reactions, no severe infections, no lymphopenia, no neutropenia)
• Confirmed preliminary efficacy in Phase 2a UC study
  • All endpoints favorable to ABX464
  • Fast onset of action
• Durability of effect :
  • Maintenance 6-month interim data
    • Partial Mayo Score continued to decrease
    • Faecal Calprotectin levels went down to values approaching normal values
  • Maintenance 9-months data confirm safety ad durability
ABX464 next steps

• Phase 2b study protocol in 232 patients with moderate to severe ulcerative colitis was submitted to regulatory agencies in first countries
  • Approved in Canada and first EU countries
  • Study open to recruitment of new sites

• Phase 2a studies are being submitted in Rheumatoid Arthritis and Crohn’s disease
## Acknowledgements

- Patients and investigators

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<tr>
<th>COUNTRY</th>
<th>PRINCIPAL INVESTIGATOR</th>
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