### Background
Multiple studies described the effectiveness of ustekinumab (UST) and vedolizumab (VDZ) in CD patients failing anti-TNFs. However, the effectiveness of VDZ or UST as a third-class biologic has not yet been described.

### Aim
We aim to investigate and compare the effectiveness of VDZ and UST as a third-class biologic in patients with CD.

### Methods
This was a retrospective multicenter cohort study. We included CD patients who received three different classes of biologicals. The primary outcome was clinical response (reduction in Harvey-Bradshaw Index (HBI) at week 16, and secondary outcomes were clinical remission (HBI < 4), C-reactive protein (CRP)-normalization, adverse events, corticosteroid-free remission, and response at both week 16 and 52.

### Results:

<table>
<thead>
<tr>
<th>Patients number, N (%)</th>
<th>Group A</th>
<th>Group B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>204 (76.47%)</td>
<td>Group A: 74 (32.21%), Group B: 66 (31.93%)</td>
<td>P = 0.699</td>
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</tbody>
</table>

### At week 16-22:
- Clinical response: 87/156 (55.2%) and 74/56 (56.2%) (p=0.70).
- Clinical remission: 41/156 (26.2%) and 15/48 (31.2%) (p=0.50).

### At week 52:
- Clinical response: 103/156 (86.4%) and 25/29 (86.2%) (p=0.9).
- Clinical remission: 31/103 (30%) and 7/29 (24.1%) (p=0.5).

### Treatment discontinued:
26/156 (17.3%) in group A and 9/48 (18.75%) in group B. The mean reason for discontinuation of treatment was clinical failure.

### Conclusion:
The current study demonstrates that administering a third-class biological therapy is effective in more than half of the patients with CD, who have already failed two biologicals of class.

No difference in effectiveness was detected between VDZ and UST as a 3rd class agent.