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AWMF-Registernr.: 021-009

**Literatursammlung:**

**Leitlinienupdate 2023**

***Inhalt:*** *2 Literaturstellen*

| Literaturstelle | Evidenzlevel | Studientyp |
|---|---|---|
| Danese, Silvio 2022 | 1 | RCT |
| D'Haens, Geert 2023 | 1 | RCT |

***OXFORD (2011) Appraisal Sheet: RCT:*** *2 Bewertung(en)*

**Danese, Silvio et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. The Lancet. 399. 2113-2128. 2022**

| Population | Intervention - Comparison | Outcomes/Results |
|---|---|---|
| **Evidence level:** 1<br><br>**Study type:** RCT<br><br>**Number of Patient:** 925<br><br>**Recruitung Phase:** 2 Jahre<br><br>**Inclusion Criteria:** Mittelschwere bis schwere CU; 16-75 Jahre, adapted Mayo score 5-9, endoscopischer Subscore 2 oder 3<br><br>**Exclusion Criteria:** Morbus Crohn. Aktive Infektion, fulminante Colitis, toxisches Megacolon, Indeterminate Colitis, Proktitis. | **Intervention:**<br>Induktion UC1: 319<br>Induktion UC2: 345<br>Erhaltung UC3: 451 (UC1 +UC2)<br><br>**Comparison:**<br>Induktion UC1: 155<br>Induktion UC2: 177<br>Erhaltung UC3: 149 (UC1 +UC2) | **Primary:** In UC1, the primary endpoint—clinical remission at<br>week 8—was achieved by 83 (26%) of 319 patients receiving upadacitinib versus seven (5%) of 154 patients receiving placebo (p<0·0001; adjusted treatment<br>difference 21·6% [95% CI 15·8–27·4]; table 3, appendix p 25). In UC2, clinical remission at week 8 was<br>achieved by 114 (33%) of 341 of patients receiving upadacitinib versus seven (4%) of 174 receiving placebo<br>(p<0·0001; adjusted treatment difference of 29·0% [95% CI 23·2–34·7]; table 3; appendix p 25). In both induction studies, clinical remission at week 8 was consistent across all subgroups (appendix pp 31–32),<br>including patient subgroups with or without previous biological failure (appendix p 45).<br><br>In UC3, the primary endpoint—clinical remission at week 52—was achieved by 63 (42%) of 149 patients receiving upadacitinib 15 mg once daily, 80 (52%) of 154 receiving upadacitinib 30 mg once daily, and 18 (12%)<br>of 149 receiving placebo (adjusted treatment difference of<br>30·7% [95% CI 21·7–39·8] for upadacitinib 15 mg vs placebo, p<0·0001; 39·0% [29·7–48·2] for upadacitinib<br>30 mg vs placebo, p<0·0001; table 4, appendix p 28). Clinical remission at week 52 was consistent across all<br>subgroups assessed in the maintenance study (appendix |

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| | | pp 33–34), including patient subgroups with or without<br>previous biological failure (appendix pp 45–46). The placebo adjusted rates for the primary endpoint of clinical remission per Adapted Mayo score were 30·7%<br>(15 mg) and 39·0% (30 mg) in overall population,<br><br>**Secondary:** All secondary endpoints in both induction studies were achieved in the upadacitinib 45 mg once daily group<br>compared with the placebo group (table 3). At week 8, disease activity and symptoms were statistically significantly<br>improved as shown by achievement of clinical response, no abdominal pain, and no bowel urgency. Endoscopic, histological, and QOL (IBDQ and FACIT-F) improvements<br>were also achieved (table 3, appendix<br>pp 25–26). The proportion of patients achieving clinical<br>response at week 2 with upadacitinib was statistically significantly greater than with placebo in both UC1 and<br>UC2 (192 [60%] of 319 vs 42 [27%] of 154 and 216 [63%] of<br>341 vs 45 [26%] of 174, respectively; both p<0·0001; table 3).<br>Consistent with clinical and endoscopic outcomes,<br>more patients treated with upadacitinib achieved faecal<br>calprotectin less than 150 mg/kg at weeks 2 and 8 of induction (appendix p 47). Greater decreases in high sensitivity CRP concentrations were demonstrated with<br>upadacitinib treatment versus placebo (appendix p 40–41).<br><br>**Results:**<br><br>**Author's Conclusion:** Upadacitinib demonstrated a positive efficacy and safety profile and could be an effective treatment<br>option for patients with moderately to severely active ulcerative colitis.<br>Funding AbbVie. |

**Methodical Notes**

**Funding Sources:** AbbVie funded trial

**COI:**

**Randomization:** 2:1

**Blinding:** blinded RCT

**Dropout Rate/ITT-Analysis:**

**Notes:**

**D'Haens, Geert et al. Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis. New England Journal of Medicine. 388. 2444-2455. 2023**

| Population | Intervention - Comparison | Outcomes/Results |
|---|---|---|
| **Evidence level:** 1<br><br>**Study type:** RCT<br><br>**Number of Patient:** 1281<br><br>**Recruitung Phase:**<br><br>**Inclusion Criteria:**<br><br>**Exclusion Criteria:** | **Intervention:** In the induction trial, patients were randomly assigned in a 3:1 ratio to receive mirikizumab (300 mg) or placebo, administered intravenously, every 4 weeks for 12 weeks.<br>In the maintenance trial, patients with a response to mirikizumab induction therapy were randomly assigned in a 2:1 ratio to receive mirikizumab (200 mg) or placebo, administered subcutaneously, every 4 weeks for 40 weeks. The primary end points were clinical remission at week 12 in the induction trial and at week 40 (at 52 weeks overall) in the maintenance trial.<br><br>**Comparison:** Placebo | **Primary:** Significantly higher percentages of patients in the mirikizumab group than in the placebo group had clinical remission at week 12 of the induction trial (24.2% vs. 13.3%, P<0.001) and at week 40 of the maintenance trial (49.9% vs. 25.1%, P<0.001).<br><br>At week 12 of the induction trial, the percentage of patients with clinical remission was higher in the mirikizumab group than in the placebo group (24.2% vs. 13.3%; difference, 11.1 percentage points; 99.875% confidence interval [CI], 3.2 to 19.1; P<0.001) (Fig. 1A). These results were similar to those for the alternative definition of clinical remission (25.6% in the mirikizumab group vs. 14.6% in the placebo group, P<0.001) and for the sensitivity analyses<br><br>**Secondary:** Results favored the mirikizumab group for the major secondary end points of clinical response, endoscopic remission, remission of symptoms at weeks 4 and 12, clinical response in patients who had previous treatment failure with a biologic agent or tofacitinib, histologic–endoscopic mucosal improvement, and bowel-movement urgency (P<0.001 for all comparisons) (Fig. 1A and 1B and Fig. S5). Depending on trial group and trial period, between 3.8 and 39.1% of the patients were classified as not having had a response owing to the discontinuation of mirikizumab or placebo or the receipt of rescue therapy with mirikizumab. Between 0 and 3.3% of the patients with sporadic missingness of data that was due to other reasons were imputed as not having had a response. The frequency of missing end-point data is summarized in Table S5.<br>In the subgroup of patients with treatment failure with a biologic agent or tofacitinib, the percentage of patients who met all the secondary end points appeared to be greater in the mirikizumab group than in the placebo group (in an analysis not adjusted for multiplicity) (Table S6 and Fig. S6). Results of all the prespecified subgroup analyses are provided in Figure S4. The Inflammatory Bowel Disease Questionnaire score (Fig. S7A and S7C) and the levels of inflammatory biomarkers C-reactive protein and fecal calprotectin (Fig. S8A and S8C) appeared to be improved in the mirikizumab group as compared with the placebo group at week 12.<br><br>**Results:**<br><br>**Author's Conclusion:** Results favored the mirikizumab group for the major secondary end points of clinical response, endoscopic remission, remission of symptoms at weeks 4 and 12, clinical response in patients who had previous treatment failure with a biologic agent or tofacitinib, histologic–endoscopic mucosal improvement, and bowel-movement urgency (P<0.001 for all comparisons) (Fig. 1A and 1B and Fig. S5). Depending on trial group and trial period, between 3.8 and 39.1% of the patients were classified as not having had a response owing to the discontinuation of mirikizumab or placebo or the receipt of rescue therapy with mirikizumab. Between 0 and 3.3% of the patients with sporadic missingness of data that was due to other reasons were imputed as not having had a response. The frequency of missing end-point data is summarized in Table S5.<br>In the subgroup of patients with treatment failure with a biologic agent or tofacitinib, the percentage of patients who met all the secondary end points appeared to be greater in the mirikizumab group than in the placebo group (in an analysis not adjusted for multiplicity) (Table S6 and Fig. S6). Results of all the prespecified subgroup analyses are provided in Figure S4. The Inflammatory Bowel Disease Questionnaire score (Fig. S7A and S7C) and the levels of inflammatory biomarkers C-reactive protein and fecal calprotectin (Fig. S8A and S8C) appeared to be improved in the mirikizumab group as compared with the placebo group at week 12. |
| **Methodical Notes** | | |

**Funding Sources:** Lilly

**COI:**

**Randomization:** 3:1

**Blinding:** yes

**Dropout Rate/ITT-Analysis:**

**Notes:**

**Versionsnummer:** **6.2**

**Erstveröffentlichung:** **11/2000**

**Überarbeitung von:** **04/2021**

**Nächste Überprüfung geplant:** **06/2023**