Serum Ustekinumab Concentrations are Associated with Improved Outcomes

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Background & Aims

- Controversy exists for ustekinumab concentrations needed in Crohn's disease (CD)
- No data exist comparing ustekinumab concentrations and validated radiologic outcomes
- We characterized these relationships and clarified concentrations needed

Methods

- CD patients on maintenance (>16 weeks) ustekinumab with both ustekinumab concentrations and simplified magnetic resonance index of activity (sMaRIA) scoring were included
- Concentrations were included if within 8 days of the next dose (and/or >4 weeks from the previous dose if q8wks)
- Repeat analyses were performed on a stricter subset of trough concentrations taken ≤ 2 days prior to next dose
- Ustekinumab concentrations were compared between those with and without (1) radiologic remission (sMaRIA< 2); (2) absence of severe radiologic inflammation (sMaRIA< 3); (3) fecal calprotectin (FCP) biomarker remission (FCP< 50µg/g)
- Area under the receiver-operating characteristic (AUROC) curve determined optimal ustekinumab concentration
- Outcomes were compared between patients above and below identified ustekinumab thresholds

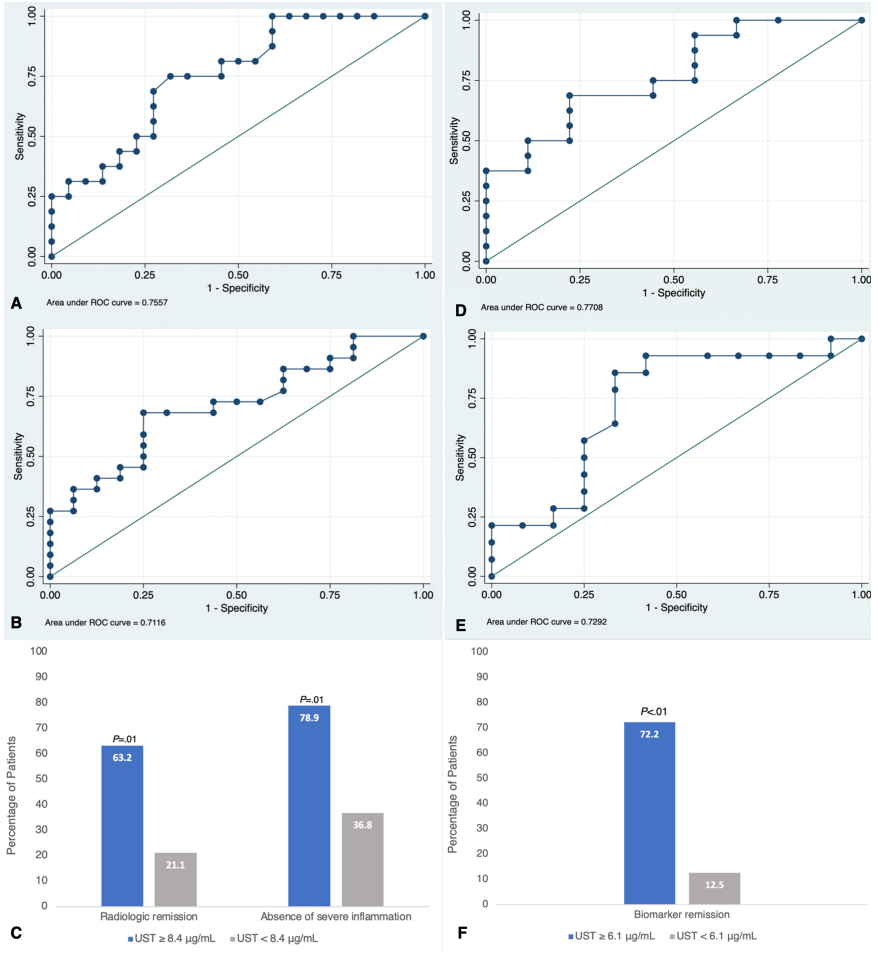

Figure 1. (A) sMARIA score of < 2, absence of any inflammation, optimal concentration is 8.4 µg/mL (area under curve, 0.76; sensitivity, 75%; specificity 68%). (B) sMARIA score of < 3, absence of severe inflammation, optimal serum concentration is 8.4 µg/mL (area under curve, 0.71). (C) Radiologic outcomes based on ustekinumab concentrations. (D) sMARIA score of < 3, absence of severe inflammation, based on ustekinumab concentrations for patients with ustekinumab concentrations ≤ 2 days prior to next dose, optimal serum concentration is 8.5 µg/mL (area under curve, 0.77). (E) Biomarker remission (FCP < 50 µg/g), optimal serum concentration is 6.1 µg/mL (area under curve, 0.73; sensitivity, 93%; specificity 58%). (F) Biomarker remission based on ustekinumab concentrations.

Results

- Thirty-eight paired ustekinumab concentrations and magnetic resonance enterography results were included
- Ustekinumab concentrations were higher with radiologic remission (11.4µg/mL vs. 6.4µg/mL, *P*=.005)
- Higher ustekinumab concentrations had good diagnostic accuracy for radiologic remission (AUROC 0.76, 95% CI 0.60 – 0.91) and for absence of severe inflammation (AUROC 0.71, 95% CI 0.55 – 0.88, optimal concentration 8.4µg/mL)
- With ustekinumab ≥8.4µg/mL, higher proportions had radiologic remission (63.2% vs. 21.1%, *P*=.01) and absence of severe inflammation (78.9% vs. 36.8%, *P*=.01) compared to patients with lower concentrations
- Ustekinumab concentrations had good diagnostic accuracy (AUROC 0.73, 95% CI 0.52 – 0.94) for FCP biomarker remission (optimal concentration: 6.1µg/mL)
- Patients with ustekinumab concentrations ≥6.1µg/mL had higher proportions with biomarker remission (72.2% vs. 12.5%, *P*<.01) compared to those with lower concentrations.

Discussion

- Ustekinumab concentrations are associated with radiologic and biomarker outcomes in CD
- These data validate the need for higher ustekinumab concentrations

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