P-013

Pregnancy Outcomes in Women Exposed to Ustekinumab in the Crohn’s Disease Clinical Development Program


BACKGROUND: Ustekinumab (UST) has been approved for moderate to severe Crohn’s Disease (CD) in adult patients (pts). While no adverse developmental outcomes (pre-8 postnatal) were observed in animal studies of UST, limited data exist including previously reported outcomes in psoriasis (Ps20) pts, concerning the effects of UST on human pregnancies1. To characterize pregnancy outcomes in women exposed to UST during pregnancy, data from the UST CD clinical development program (CDP) are presented.

METHODS: Maternal and fetal outcomes with maternal use of UST (typical terminal half-life of approx 3 weeks) from 5 CD studies were evaluated: Phase 2: Phase 2 (CDST7970: n=113, CERTI+0.0125) & Phase 3 (UNIT1-1: n=789, CERTI+0.0125) for which 1,281 controls were matched 1:1. The primary endpoint was live births. Mean maternal age was 33.0±2.9 years vs. 27.6±3.7 years and median UST treatment duration was longer for pts who had SaS (80 weeks) vs. LBs (56 weeks). Among the pts, there were no congenital anomalies; 1 infant had a single episode of transient hypoglycemia treated with oral supplemental formula. No safety signals emerged with neonatal outcomes with gestational age of 38.2±1.6 weeks (n=12), mean 5-min APGAR of 8.9±1.95 (n=12), and a 6.1±0.6% cesarean delivery rate.

CONCLUSION(S): While the rate of SaS was generally comparable to the rate previously reported in Ps20 data, the small number of pregnancies among women with CdP exposure to UST precludes definitive interpretation of the data. In this case series, SaS were associated with older maternal age, and longer duration of UST exposure prior to the reported pregnancy was not associated with adverse outcomes. However, the limited available data from the UST CD program requires additional research to determine pregnancy and newborn safety.


P-014

Ustekinumab IV Induction Results in Crohn’s Disease Symptom Improvement Within the First Week in Anti-TNF Refractory Patients

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BACKGROUND: In both the UNIT 1&2 Crohn’s disease (CD) studies, a single 6mg/kg Ustekinumab (UST) IV infusion showed significantly greater rates of clinical response & remission vs placebo, and significant reductions in CDAI (and -70 pt reduction) by the first post-baseline visit at Wk 21. It remains to be determined how soon patients see benefit (ie. before Wk 3).

METHODS: Patients (pts) ≥18 yrs, who had moderate to severe UC who achieved remission at Wk 2 (CDST7970: n=144; UNIT1-1: n=168) for which 300 controls were matched 1:1, were given 6mg/kg UST IV weekly for 5 weeks. Data from the first 4 pts were missing from available efficacy data (daily 7-14 days prior). The primary endpoint was mean change in CDAI from baseline to Wk 5. The rate of SaS was 6.9% of pts who had SaS vs 1.3% of pts who had SaS (p=0.044).

RESULTS: IV UST induced significant improvement in all 3 components of CDAI at 21 days (ΔCDAI=-128 vs placebo, ΔCDAI=-31 vs placebo at Wk 3). The treatment benefit was seen as early as Wk 1 for pts who had SaS (vs placebo) (ΔCDAI=-65 vs placebo, ΔCDAI=-17 vs placebo at Wk 3). Rank ordinal response was used to compare groups for all analyses. A p-value of 0.05 or less was considered statistically significant. Based on the analysis of the primary endpoint, treatment was considered a success in 59% of pts who had SaS at Wk 5 compared to 41% of pts who had SaS at Wk 5. All pts who reached remission at Wk 5 remained in remission at Wk 30. SaS was associated with older maternal age, and longer duration of UST exposure prior to the reported pregnancy was not associated with adverse outcomes. However, the limited available data from the UST CD program requires additional research to determine pregnancy and newborn safety.


P-015

Maintenance of Remission with Tofacitinib in Patients With Ulcerative Colitis: Subpopulation Analysis from an Open-Label, Long-Term Extension Study


BACKGROUND: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib was demonstrated in three Phase 3, randomized, placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458953; OCTAVE Sustain, NCT01458574) in patients with moderate to severe UC.1 An ongoing Phase 3, multicenter, open-label, long-term extension study (OLE: NCT01470662) included subjects rolling over from OCTAVE induction 1 or 2, or OCTAVE Sustain. We present data from the cohort of patients who were previously in remission at the end of OCTAVE induction 1 or 2, and who were maintained on tofacitinib 5 mg twice daily (BID) in the OLE study. Remission and mucosal healing (Mayo endoscopic subscore of 0 or 1 at month 2 and 12, based on local-read, assessment, are presented. Safety data up to 3 years of treatment (as of July 8, 2016) are reported for all patients who received tofacitinib 5 mg BID in the OLE study.

RESULTS: Of 914 patients enrolled in the OLE study (mean age: 45 years old; gender: 47.2% female) were in remission, based on central endoscopic reading, at Week 52 of OCTAVE Sustain. Of these, 58.7% reported tofacitinib 5 mg twice daily (BID) as the most effective treatment, and 15.0% (47.6%) discontinued in the OLE study (reasons included: study-related adverse event [AE], n=4; infusion and local-read, assessment, are presented. Safety data up to 3 years of treatment (as of July 8, 2016) are reported for all patients who received tofacitinib 5 mg BID in the OLE study.

METHODS: Patients in remission (Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore ≤0) at Week 52 of OCTAVE Sustain were to receive tofacitinib 5 mg twice daily (BID) in the OLE study. Remission and mucosal healing (Mayo endoscopic subscore of 0 or 1 at month 2 and 12, based on local-read, assessment, are presented. Safety data up to 3 years of treatment (as of July 8, 2016) are reported for all patients who received tofacitinib 5 mg BID in the OLE study.

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CONCLUSION(S): The majority of patients with moderate to severe UC who achieved remission at Week 52 of OCTAVE Sustain maintained remission and mucosal healing with tofacitinib 5 mg BID, over time, up to 12 months in the OLE study. Compared with OCTAVE Sustain, no new safety concerns associated with long-term exposure to tofacitinib emerged in this subpopulation.