2023. U-EXCEL
U-EXCEED
U-ENDURE

RCT/Upadacitinib/CD/ Induction

Upadacitinib Induction and Maintenance Therapy for Crohn's Disease

Two phase 3 induction trials (U-EXCEL & U-EXCEED) & maintenance. Patients with mod-severe CDwere randomized to 45mg/day of UPA vs placebo for 12 weeks. Patients with clinical response were randomized in U-ENDURE trial to 15mg UPA vs 30mg UPA vs pbo.

Primary endpoints: clinical remission (CDAI <150) and endoscopic response (↓ of >50% of SES-CD from baseline) at w12 and w52.

Results: **U-EXCEL N=526; U-EXCEED N= 495 & U-ENDURE N=502**

- Clinical remission after induction:
  - U-EXCEL 49.5% UPA vs 29.1% placebo, p<0.0001
  - U-EXCEED 38.9% UPA vs 21.1% placebo, p<0.0001
- Endoscopic response after induction:
  - U-EXCEL 45.5% UPA vs 13.1% placebo, p<0.0001
  - U-EXCEED 34.6% vs 3.5%, p<0.0001
- At week 52, clinical remission U-ENDURE was 37.3% UPA15 vs 47.6% UPA30 vs 15.1% placebo, p<0.0001
- At week 52 endoscopic response: 27.6% UPA15 vs 40.1% UPA30 vs 7.3% placebo, p<0.0001
- Herpes zoster, hepatic disorders more freq in UPA than placebo.

Conclusion:
Upadacitinib induction and maintenance treatment was superior to placebo in patients with moderate-to-severe Crohn's disease.

Table 2. Primary and Key Secondary End Points under Multiplicity Control for Upadacitinib as Induction Therapy, According to FDA Requirements.*

End Point	U-EXCEL Induction Trial (12 wk)			U-EXCEED Induction Trial (12 wk)		
	Placebo (N=176)	Upadacitinib, 45 mg (N=350)	Adjusted Difference; P Value†	Placebo (N=171)	Upadacitinib, 45 mg (N=324)	Adjusted Difference; P Value†
Primary end points — % (95% CI)						
CDAI clinical remission‡	29.1 (22.4 to 35.8)	49.5 (44.2 to 54.8)	20.8 (12.7 to 28.8); P<0.001	21.1 (14.9 to 27.2)	38.9 (33.6 to 44.2)	17.9 (10.0 to 25.8); P<0.001
Endoscopic response§	13.1 (8.1 to 18.0)	45.5 (40.3 to 50.8)	33.0 (26.2 to 39.9); P<0.001	3.5 (0.8 to 6.3)	34.6 (29.4 to 39.8)	31.2 (25.5 to 37.0); P<0.001

Table 3. Primary and Secondary End Points under Multiplicity Control for Upadacitinib as Maintenance Therapy, According to FDA Requirements.*

End Point, Wk 52	Placebo (N=165)	Upadacitinib, 15 mg (N=169)	Adjusted Difference vs. Placebo; P Value†	Upadacitinib, 30 mg (N=168)	Adjusted Difference vs. Placebo; P Value†
Primary end points — % (95% CI)					
CDAI clinical remission‡	15.1 (9.6 to 20.6)	37.3 (30.0 to 44.6)	23.7 (15.2 to 32.1); P<0.001	47.6 (40.1 to 55.2)	32.8 (23.9 to 41.6); P<0.001
Endoscopic response§	7.3 (3.3 to 11.2)	27.6 (20.8 to 34.4)	21.0 (13.6 to 28.4); P<0.001	40.1 (32.7 to 47.6)	33.7 (26.0 to 41.3); P<0.001

Patients at U-EXCEL had a history of failing ≥1conventional or biological therapies; those in U-EXCEED had failed ≥1 biologics.

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