Biosimilar Infliximab (CT-P13) is Not Inferior to Originator Infliximab: Results from a 52-week Randomized Switch Trial in Norway

Abstract 19LB

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Abstract

Background/purpose:
TNF-inhibitors (TNFi) have improved treatment of spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA), Crohn's disease (CD), ulcerative colitis (UC), and chronic plaque psoriasis (Ps). The NOR-SWITCH trial was funded by the Norwegian government. The aim of the NOR-SWITCH trial was to examine switching from originator to biosimilar infliximab regarding efficacy, safety and immunogenicity.
Methods:
The study was designed as a 52-week randomized, double-blind, non-inferiority, phase IV trial. Adult patients with a diagnosis of SpA, RA, PsA, CD, UC or Ps on stable treatment with the originator infliximab (Remicade®, INX) for at least 6 months were eligible. Patients with informed consent were randomized 1:1 to either continued INX or switch to CT-P13 treatment (biosimilar infliximab, Remsima®), using unchanged dosing regimen. Data were collected at infusion visits. The primary endpoint was disease worsening during follow-up according to worsening in disease-specific composite measures and/or a consensus between investigator and patient leading to major change in treatment. Exploratory subgroup analyses were performed to examine disease worsening within each of the six diagnoses. The non-inferiority margin was set to 15% and power calculations indicated that 394 patients were required in the primary Per Protocol Set (PPS). The primary endpoint was analysed using logistic regression, adjusted for diagnosis and disease duration at baseline.
Results
Between October 6, 2014 and July 8, 2016, 481 patients (INX 241, CT-P13 240, Full Analysis Set, FAS) at 40 Norwegian study centres were randomized, received treatment and were followed for 52 weeks. The main demographic and baseline characteristics are shown in the table. Disease worsening occurred in 26.2% and 29.6% of patients in the INX and CT-P13 arms, respectively (PPS). The 95% confidence interval of the adjusted treatment difference (-4.4%) was -12.7 – 3.9 which was within the pre-specified non-inferiority margin. The frequency of disease worsening in each specific diagnosis is shown in the table (exploratory analyses). Changes in the generic disease variables and disease specific composite measures were similar in both arms (table). The incidence of anti-drug antibodies detected during the study was 17 (7.1%) and 19 (7.9%) in the INX and CT-P13 patients, respectively (FAS). The trough drug levels and the frequencies of reported adverse events including infusion reactions were also similar (data not shown).
Conclusion
The NOR-SWITCH trial demonstrated that switch from INX to CT-P13 was not inferior to continued treatment with INX. …

Background and objective

TNF-inhibitors (TNFi) have improved treatment of spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA), Crohn's disease (CD), ulcerative colitis (UC), and chronic plaque psoriasis (Ps). Patients starting biologic treatment can receive biosimilar CT-P13 in many countries. However, switching stable patients who are doing well on originator infliximab, has been controversial. The NOR-SWITCH trial was funded by the Norwegian government.

The aim of the NOR-SWITCH trial was to examine switching from originator to biosimilar infliximab regarding efficacy, safety and immunogenicity in patients on stable treatment with the originator drug.

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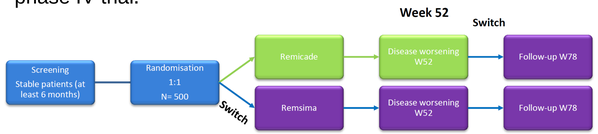
Methods

Design: 52-week randomized, double-blind, non-inferiority, phase IV trial.



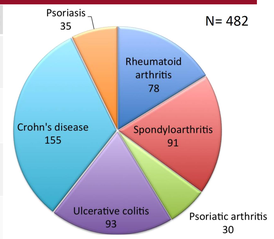
Main inclusion criteria: Adult patients with a diagnosis of SpA, RA, PsA, CD, UC or Ps on stable treatment with the originator infliximab (Remicade®, INX) for at least 6 months.

Primary endpoint: Disease worsening during follow-up according to worsening in disease-specific composite measures and/or a consensus between investigator and patient leading to major change in treatment. Exploratory subgroup analyses were performed to examine disease worsening within each of the six diagnoses.

Statistics: Non-inferiority margin 15% and power calculations indicated that 394 patients were required in the primary Per Protocol Set (PPS). The primary endpoint was analysed using logistic regression, adjusted for diagnosis and disease duration at baseline.

Results – patients

	Total	INX	CT-P13
Screened	498		
Randomised	482	241	241
Full Analysis Set (FAS)	481	241	240
Per Protocol Set (PPS)	408	202	206



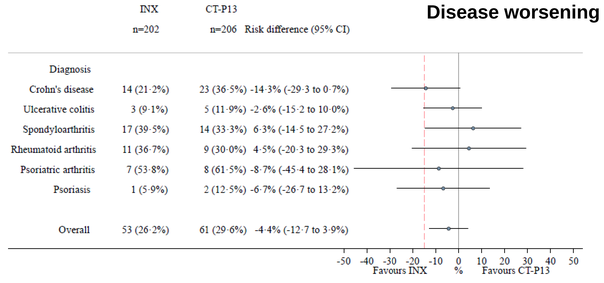
Results – patients

	INX (n=241)	CT-P13 (n=240)
Age (years)	47.5 (14.8)	48.2 (14.9)
Females (%)	41.1	36.2
Disease duration (years)	16.7 (10.9)	17.5 (10.5)
Duration of ongoing INX (years)	6.7 (3.6)	6.9 (3.8)

Numbers are mean (SD) or percent

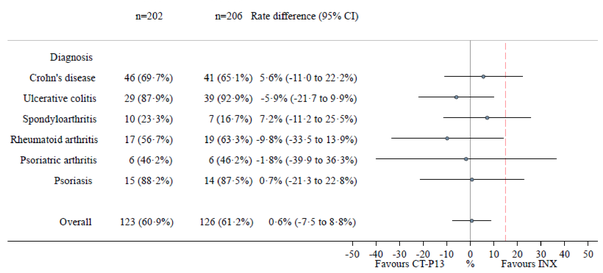
Results – primary endpoint

Disease worsening

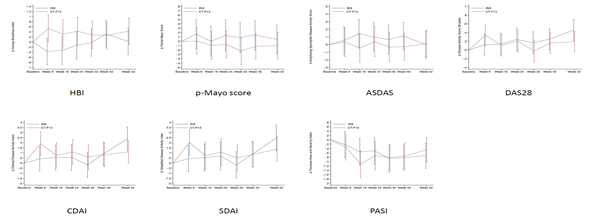


Results – secondary efficacy endpoints

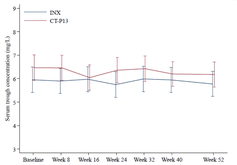
Remission



Results – secondary efficacy endpoints



Results – immunogenicity



	INX (n=241)	CT-P13 (n=240)
ADAb at any time point	10.8 %	12.5 %
Incidence of ADAb	7.1 %	7.9 %

Results – safety

[number of events] n (%)	INX (241)	CT-P13 (n=240)
SUSAR	0	0
SAE	[32] 24 (10.0)	[27] 21 (8.8)
AE	[422] 168 (69.7)	[401] 164 (68.3)
AE study drug discontinuation	[18] 9 (3.7)	[9] 8 (3.3)

Conclusion

Switch from INX to CT-P13 was not inferior to continued treatment with INX for disease worsening. Results were also similar for other efficacy endpoints, immunogenicity and safety. We recommend caution in generalizing these findings to other biologic agents. In our opinion, there is a need for further switch studies which may be extended to include multiple sequenced as well as back-and-forth switches.

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Disclosures: GL Goll Orion Pharma, Pfizer, Abbvie, Novartis IC Olsen, None KK Jorgensen Intercept, Celltrion, Tillott M Lorentzen None N Bolstad None EA Haavardsholm AbbVie, UCB, Pfizer, MSD, Roche KEA Lundin Orion Pharma, MSD, Takeda C Mork Novartis, LEO Pharma, ACO hud, AbbVie, Galderma Nordic, Cellgene J Jahnsen Orion Pharma ,Celltrion, Pfizer, MSD, AbbVie, Takeda, Napp Pharm, AstroPharma T K Kvien Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lily, Epirus, Hospira, Merck-Serono, Novartis, Orion Pharma, Pfizer, Sandoz, UCB