

Immunosuppressive co-treatment with Infliximab and Adalimumab is not superior than anti-TNF monotherapy to prevent treatment failure over time

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OBJECTIVE

In Crohn's disease there is clear benefit from combination therapy with Infliximab (IFX) and immunosuppressive drugs (IS), while the benefit is limited for Adalimumab (ADA). Although some studies suggest a benefit of combination therapy with IFX in ulcerative colitis (UC) few data are available. Our aim was to assess the efficacy of anti-TNF monotherapy (IFX and ADA) and anti-TNF+IS for maintenance therapy in UC.

DESIGN

Retrospective study of patients with UC treated with IFX or ADA in Liège, Belgium. Treatment periods were divided into 6-month semesters. A combination therapy semester was defined as anti-TNF+IS for at least 3 months, a semester as anti-TNF withdrawal for secondary loss of response, intolerance or surgery. Treatment optimisation during semester was defined as dose escalation or starting steroids. Semesters with and without flares and with or without optimisation were compared through univariate and multivariate analysis. Patients receiving > 6 months anti-TNF+IS during the first semesters were separately analysed.

RESULTS

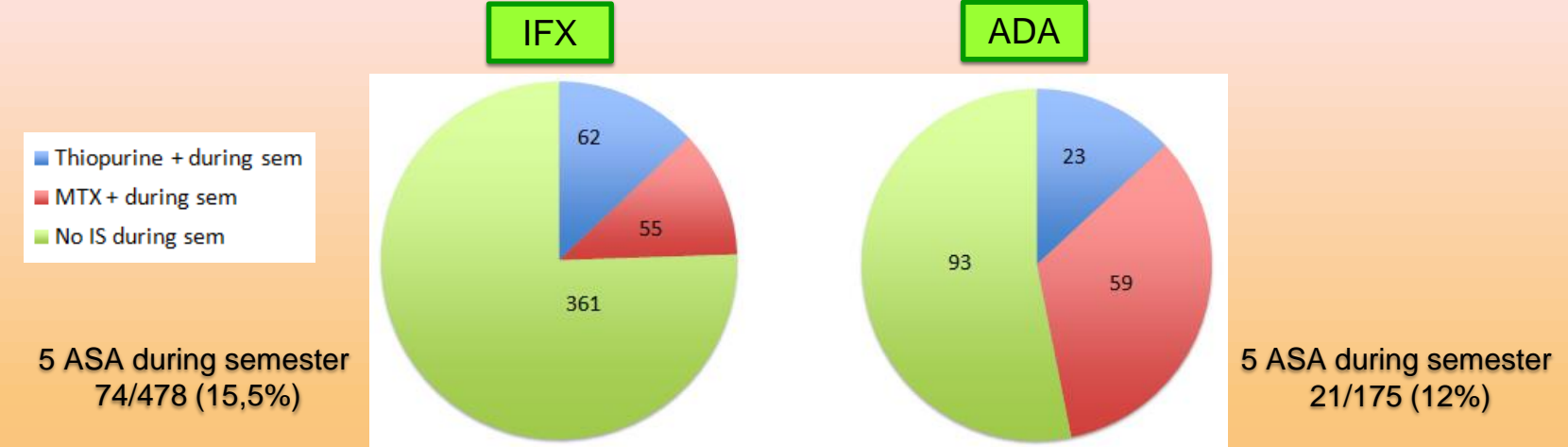
478 semesters in 60 patients with IFX and 175 semesters in 33 patients with ADA were included for the maintenance analysis. The mean IFX and ADA treatment duration were respectively 49 (±33) months and 38 (±19) months. Within patients treated with IFX, 32/60 patients received IFX+IS during the first semester. IFX was administrated as monotherapy in 361/478 semesters (76%) and as combination therapy in 117/478 semesters (24%). 90% and 34% of semesters with IFX required dose escalation and corticosteroids course respectively. IFX+IS was associated with more semesters with failure (5% vs 3%, p=0.02). IS+IFX was not associated with less semesters with dose escalation (64% vs 31%, p=0.06) or corticosteroids use (p=0,63). IS during the first semester was not associated with lower risk of IFX failure (p=0.41) nor with a higher survival without IFX withdrawal (p=0.20). Continuing the IS treatment beyond the first semester was not associated with fewer semesters with failure (p=0.18). Within patients treated with ADA, 19/33 patients received IFX+IS during the first semester. ADA was administrated as monotherapy in 93/175 semesters (53%) and as combination therapy in 82/175 semesters (47%). 86% and 46% of semesters with ADA required dose escalation and corticosteroids course respectively. ADA+IS was not associated with less semesters with failure (7% vs 5%, p=0.58), less semester with corticosteroids use (p=0,63). More semesters with ADA+IS required ADA dose escalation (60% vs 30%, p=0,01). IS during the first semester was not associated with lower risk of ADA failure (p=0.84) nor with a higher survival without ADA withdrawal (p=0.78). Continuing the IS treatment beyond the first semester was not associated with fewer semesters with failure (p=0.20).

CONCLUSION

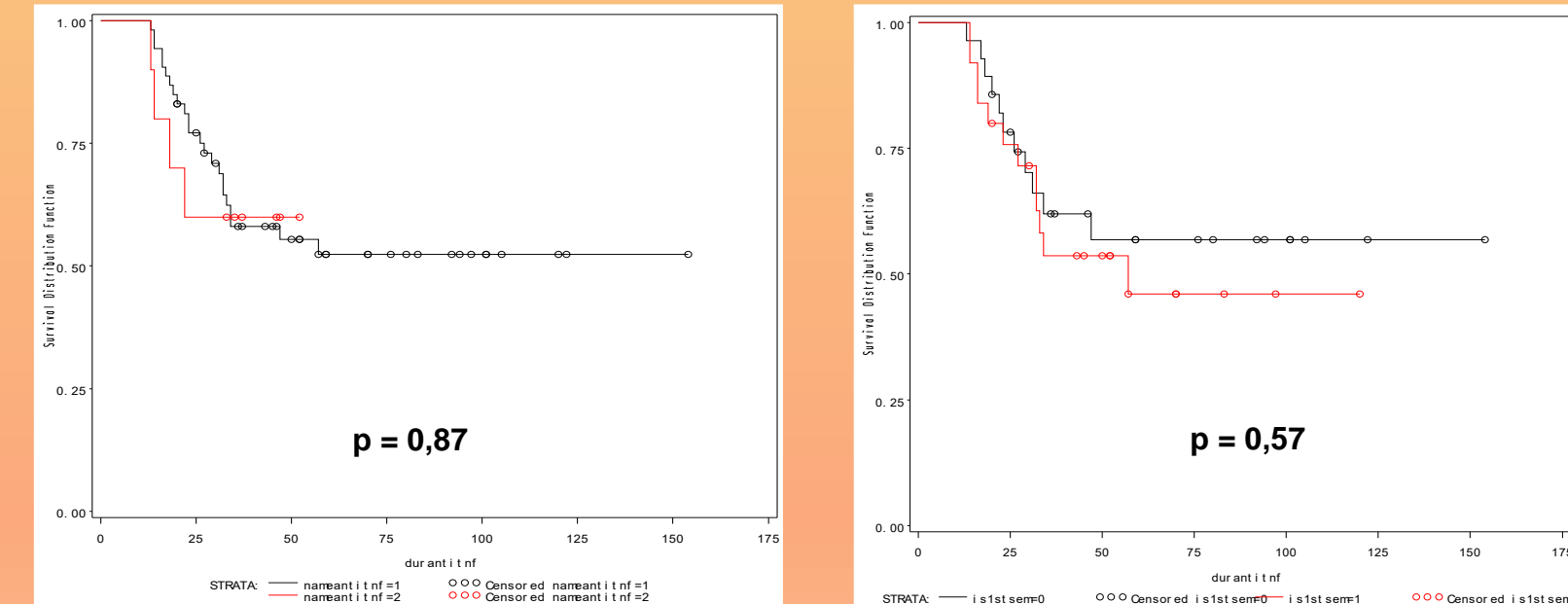
Anti-TNF+IS did not decrease IFX and ADA failure other time. Anti-TNF+IS during the first semester was not associated with lower anti-TNF failure nor longer treatment duration over time. Dose escalation with IFX and ADA was necessary in more than 85% of the patients.

| Patients Characteristics | | All patients (n=93) (%) | Patients IFX (n=60) (%) | Patients ADA (n=33) (%) |
|-------------------------------------|---------------------|-------------------------|-------------------------|-------------------------|
| Male gender | | 47 (50) | 30 (50) | 17 (51,5) |
| CHU center | | 84 (90) | 55 (91,7) | 29 (87,9) |
| Age at diagnosis (years, median±SD) | | | 32±15 | 28±16 |
| Age Montreal | A1 | 6 (6,4) | 3 (5) | 3 (9,1) |
| | A2 | 61 (65,6) | 40 (66,7) | 21 (63,6) |
| | A3 | 26 (27,9) | 17 (28,3) | 9 (27,3) |
| Extension disease at diagnosis | E1 | 18 (19,3) | 12 (20) | 6 (18,2) |
| | E2 | 56 (60,2) | 37 (61,7) | 19 (57,6) |
| | E3 | 19 (20,4) | 11 (18,3) | 8 (24,2) |
| Smoking | Never | 61 (65,6) | 36 (60) | 25 (75,8) |
| | Yes | 8 (8,6) | 7 (11,7) | 1 (3) |
| | No | 24 (25,8) | 17 (28,3) | 7 (21,2) |
| Family | No | 80 (86) | 51 (85) | 29 (87,9) |
| | 1st degree | 4 (4,3) | 3 (5) | 1 (3) |
| | > 1st degree | 9 (9,6) | 6 (10) | 3 (9,1) |
| IFX before semester | | 26 (27,9) | 3 (5) | 23 (69,7) |
| IFX: reason stop | Primary no response | 5 (20) | 0 (0) | 5 (22,7) |
| | Loss of response | 8 (32) | 1 (33,3) | 7 (31,8) |
| | Intolerance | 1 (4) | 1 (33,3) | 0 (0) |
| | Infusion reaction | 6 (24) | 0 (0) | 6 (27,3) |
| | Infection | 1 (4) | 0 (0) | 1 (4,5) |
| | Other | 4 (16) | 1 (33,3) | 3 (13,6) |
| ADA before semester | | 2 (2) | 2 (3,3) | 0 (0) |
| ADA: reason stop | Primary no response | 2 (100) | 2 (100) | 0 (0) |
| | Loss of response | 0 (0) | 0 (0) | 0 (0) |

IS DURING SEMESTER



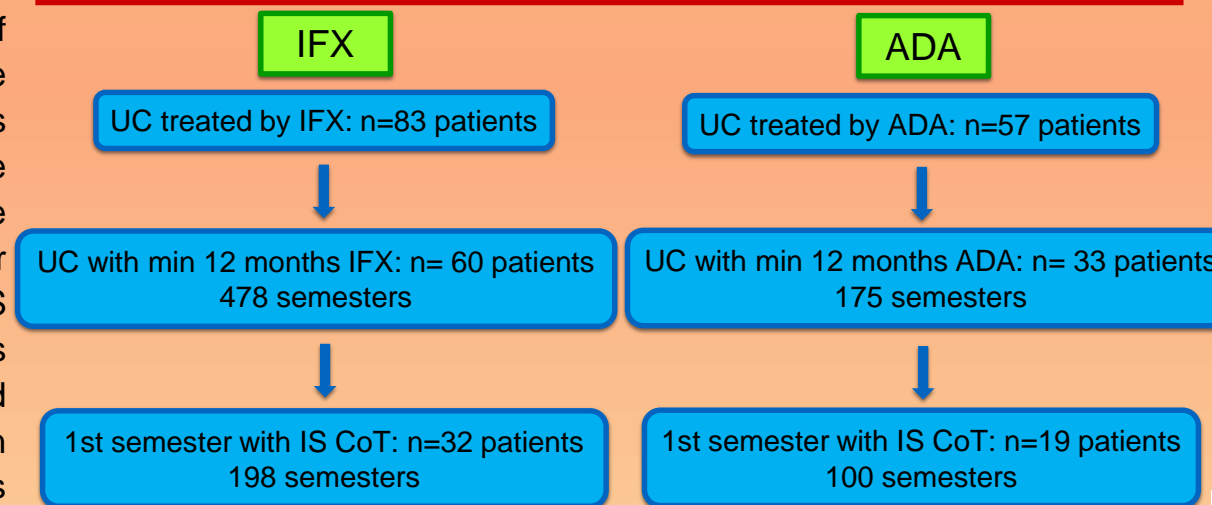
SURVIVAL WITHOUT IFX/ADA WITHDRAWAL



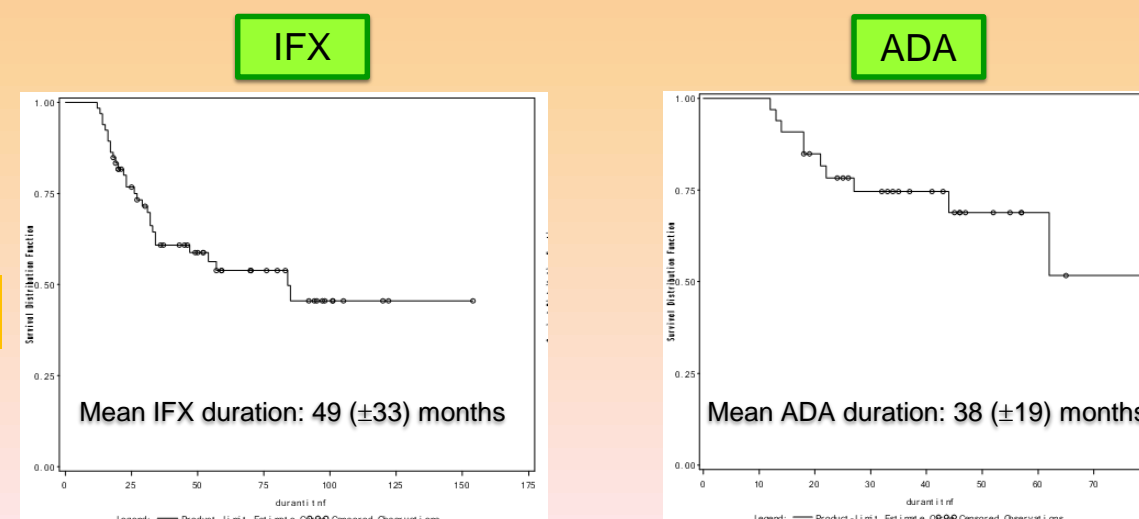
Survival without IFX/ADA withdrawal for 1st anti-TNF treatments. Comparison of IFX vs. ADA

Survival without IFX/ADA withdrawal for 1st anti-TNF treatments. Comparison of IS during 1st semester vs. without IS during 1st semester

PATIENTS DISPOSAL



SURVIVAL WITHOUT ANTI-TNF WITHDRAWAL



SEMESTERS WITH FAILURE

