# Management of infliximab refractory immune checkpoint inhibitor gastrointestinal toxicity: A multicentre case series

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## Background

- Immune checkpoint inhibitor (ICI) GI toxicity is a major cause of morbidity and, rarely, treatment-related death[1]
- Infliximab (IFX) is standard management for steroid refractory cases[2]
- Optimal management on IFX refractory tox (IRIGItox) is unknown

## Objectives

- Estimate the prevalence of patients with GI toxicity who are both steroid and IFX refractory (MIA cohort)
- Describe the investigation and management IRIGItox
- Assess the efficacy of post IFX interventions
- Assess survival outcomes stratified by post IFX intervention

## Methods

- International retrospective case series
- Data extracted regarding demographics, steroid use, response and survival.
- Incidence of IRIGItox estimated in primary cohort (MIA, Australia)



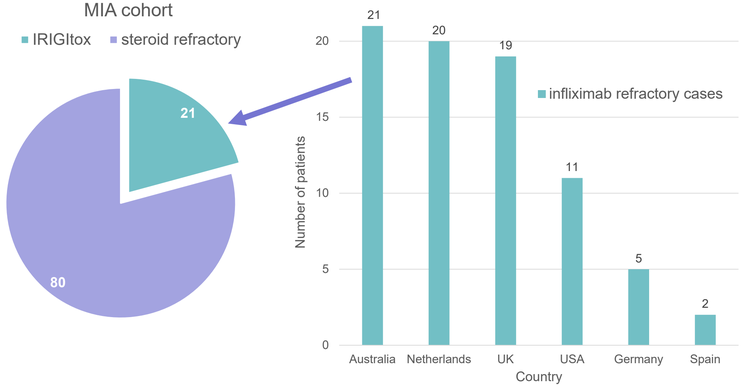


***Figure 1***: IRIGItox Cases by country, prevalence IRIGItox MIA

## Results

- N= 78 pts were identified (Figure 1).
- 21 /101 (21%) of pts who received IFX met the definition of IRIGItox (MIA cohort)
- Baseline characteristics shown in Table 1.
- GI toxicity data shown in Table 2.
- Across all pts, 106 post infliximab treatments were given. Type of post IFX treatment is shown in Table 3.

| Variable | N=78 |
|---|---|
| Age, median (range) | 60 (31, 87) |
| Male, n (%) | 44 ( 56%) |
| Melanoma, n (%) | 70 ( 90%) |
| Treatment setting, n (%)<br>- Neo-adjuvant<br>- Adjuvant<br>- Metastatic | <br>6 (8%)<br>17 (22%)<br>55 (70%) |
| Index ICI n (%)<br>- CTLA4/ PD1<br>- PD1<br>- CTLA4 | <br>50 (65%)<br>18 (23%)<br>9 (12%) |

***Table 1*** : Baseline characteristics

| Toxicity Variables | |
|---|---|
| Colitis, n (%) | 75 (96%) |
| Max CTCAE grade<br>- 2<br>- 3<br>- 4<br>- 5 | <br>4 (5%)<br>49 (63%)<br>18 (23%)<br>7 (9%) |
| time to onset colitis, days, median, (range) | 40.5 (0, 509) |
| Time to steroids, days, median (range) | 3 (0, 50) |
| Max steroid dose*, median (range) | 100 (30, 1250) |
| Primary refractory, n (%) | 46 (59%) |
| Time to infliximab dose 1, days, median (range) | 18 (1, 387) |
| Infliximab doses, median (range) | 2 (1, 6) |

***Table 2***: IRIGItox data * Prednisolone dose equivalent (mg)

| Post IFX treatment type | n |
|---|---|
| Antimetabolites<br>- Mycophenolate<br>- Azathioprine | 27<br>- 25<br>- 2 |
| Calcineurin inhibitor<br>- Ciclosporin<br>- Tacrolimus | 31<br>- 16<br>- 15 |
| Non TNF<br>- Ustekinumab<br>- tocilizumab<br>-Vedolizumab<br>- tofacitinib | 20<br>- 3<br>- 1<br>- 15<br>- 1 |
| Non systemic immunomodulatory<br>- Mesalazine<br>- Budesonide<br>- Beclomethasone<br>- ganciclovir | 16<br>- 4<br>- 3<br>- 6<br>- 3 |
| Interventional<br>- Total colectomy<br>- Partial colectomy<br>- Extra-corporeal photophoresis<br>- Faecal transplant | 7<br>- 2<br>- 3<br>- 1<br>- 1 |
| nil | 5 |

***Table 3***: Post IFX treatments

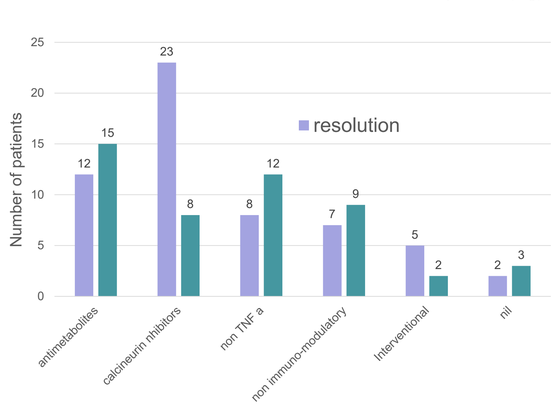


***Figure 2***: Resolution by post IFX treatment

- Calcineurin inhibitors and intervention approaches were most likely to result in toxicity resolution (23 (74%), 5 (71%)) (Figure 2).
- Time to resolution and time to steroid wean was shortest for calcineurin inhibitors (Figure 3).

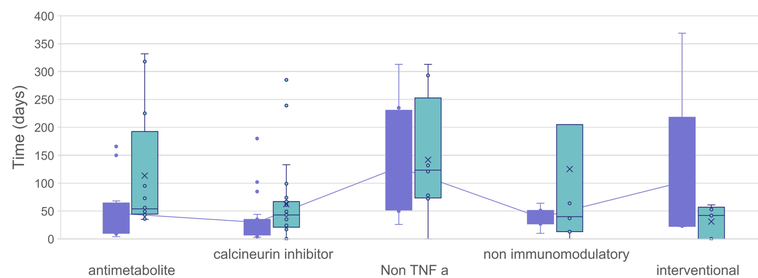


***Figure 3***: By post IFX treatment:time to resolution (days); time to steroid wean (days)

- Exploratory overall survival data is shown in Figure 4.
- Nil intervention, calcineurin inhibitors and antimetabolites exhibited a trend to poorer OS

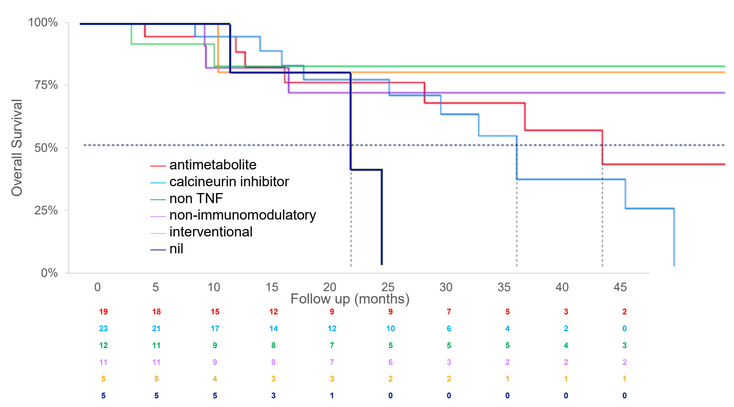


***Figure 4***: Overall survival by post IFX treatment

## Conclusions

- 1 in 5 patients with steroid refractory ICI GI toxicity are also refractory to infliximab
- Management is heterogeneous
- Calcineurin inhibitors are most likely to result in toxicity resolution and the quickest time to steroid wean
- However, calcineurin inhibitors are associated with poorer overall survival

## References

1. Wang DY, et al *JAMA Oncol.* 2018
2. Schneider BJ et al *JCO.* 2018

## Acknowledgements

- Patients and families who contributed to the case series
- International collaborators who contributed to the dataset





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