Final Results of an Open Label Phase 2 Study of a Reversible B Cell Inhibitor, XmAb®5871,in IgG4-Related Disease

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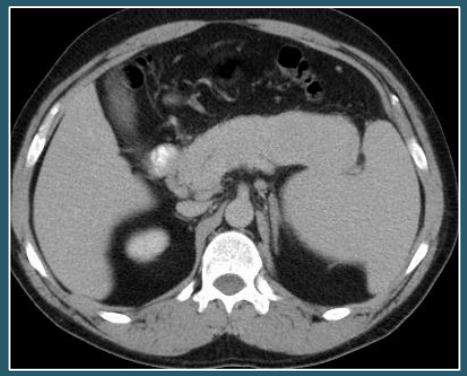

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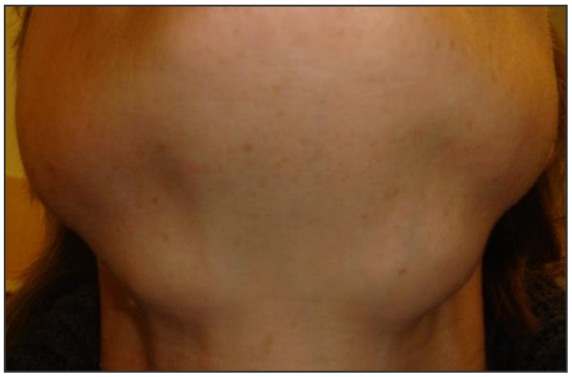
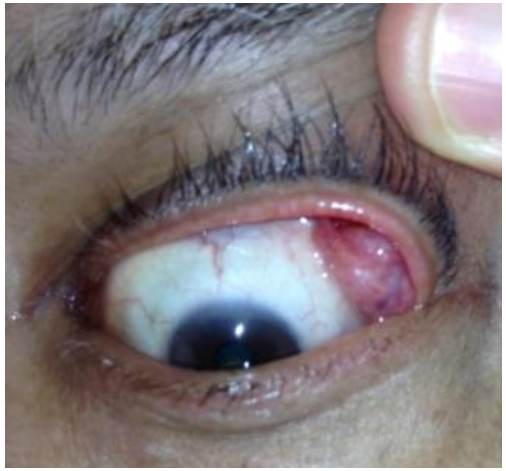
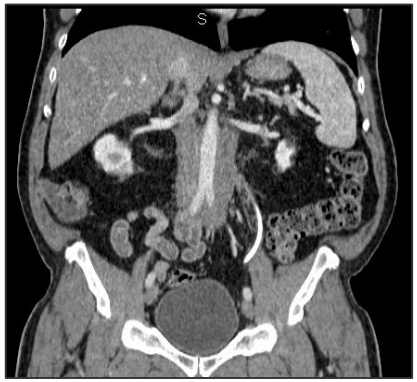
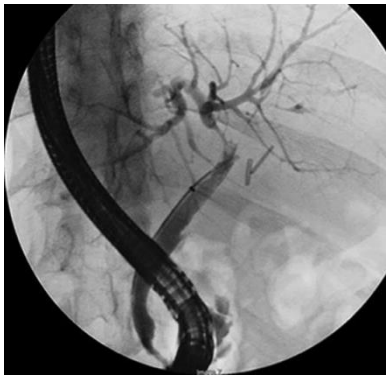
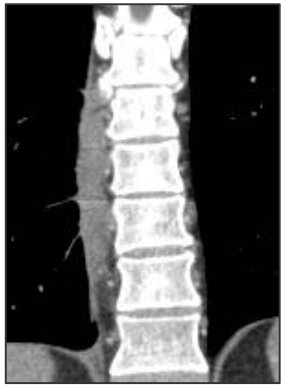
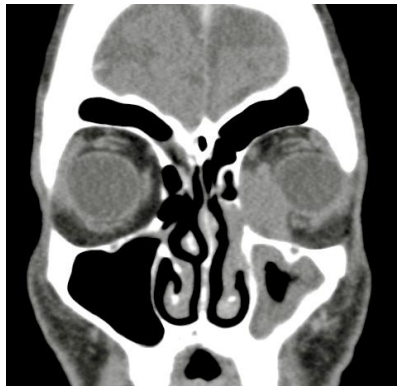
Conflicts of Interest

- Dr. Stone has received research funding from Xencor on the subject of IgG4-related disease.
- Drs. Zack and Foster are full-time employees of Xencor, Inc. and hold stock and stock options.

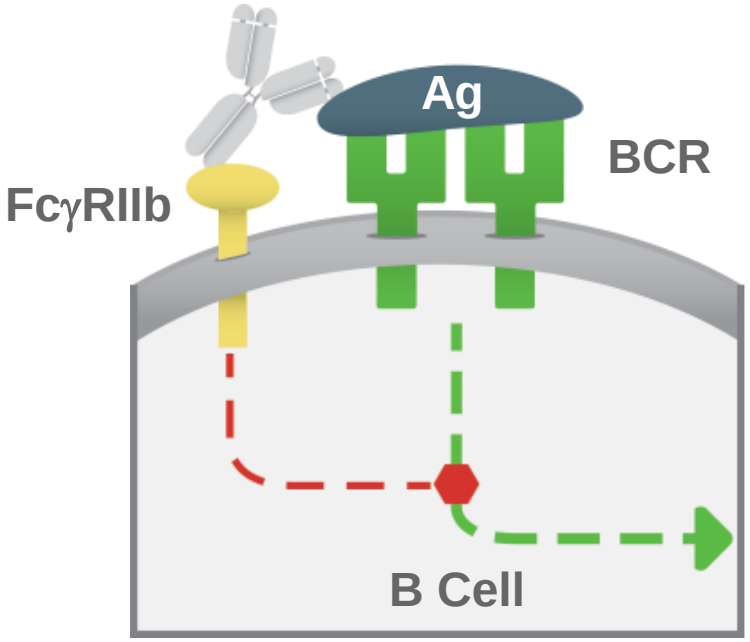



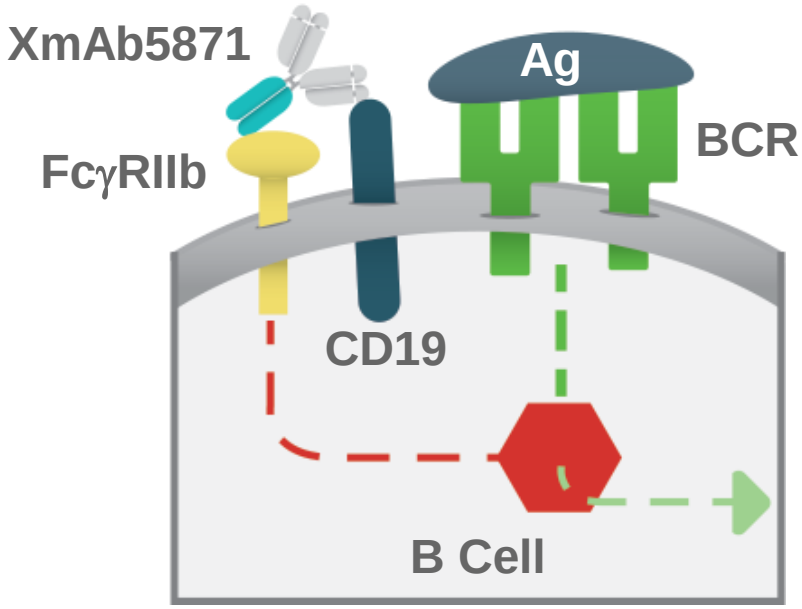
Mimicker of Sjögren's syndrome, granulomatosis with polyangiitis, lupus, Takayasu's arteritis, sarcoidosis, lymphoma, idiopathic membranous glomerulonephropathy

XmAb®5871 Enhances Natural Regulatory Role of FcγRIIb

Natural:
Ag + αAg Immune Complex



XmAb5871:
anti-CD19 with Immune Inhibitor Fc domain



- **Inhibits many activation pathways in both healthy and diseased B cells**
- **Potent suppression of B-cell responses without destroying B cells**

XmAb5871-03: Phase 2 Pilot Trial in IgG4-RD

- **Design:**
  Open-label, multiple-dose trial
  12 doses over six months

- **Study Drug Dose:**
  5 mg/kg of XmAb5871 IV q 14 days

- **Study Population**:
  Histopathologically-proven, active IgG4-RD:
  - Disease activity in one or more organ systems AND
  - IgG4-RD RI of ≥ 3

- **Numbers:**
  15 patients with active IgG4-RD

XmAb5871-03 Phase 2 Pilot Study in IgG4-RD

Primary Objective

- To evaluate the effect of XmAb5871 on the IgG4-RD Responder Index (RI) in patients with active IgG4-RD.
- **Primary endpoint:**
  Proportion of patients on Day 169 (2 weeks after 12th infusion) with decrease in IgG4-RD RI of ≥ 2 points from baseline.

Secondary Objectives

- Safety, tolerability, pharmacokinetics, immunogenicity
- **Secondary endpoint:**
  - Proportion of patients with remission on Day 169 (RI=0 and no corticosteroids after 2 months)
  - Proportion of patients with ≥ 2 points decrease in IgG4-RD RI from Day 1 at any time

IgG4-Related Disease Responder Index

- Based on the Birmingham Vasculitis Activity Scale/ANCA-Associated Vasculitis Scale (BVAS/AAV)
- Investigator scores 25 potential organ domains of activity
- Cumulative sum of organ scores provides the total RI score
- Disease-related damage also captured but scored separately

Demographics and Disease Characteristics

Demographics (N=15)

Age	Years, median (range)	63 (43 - 77)
Sex	Male Female	10 5
Race	White Asian Black	12 2 1

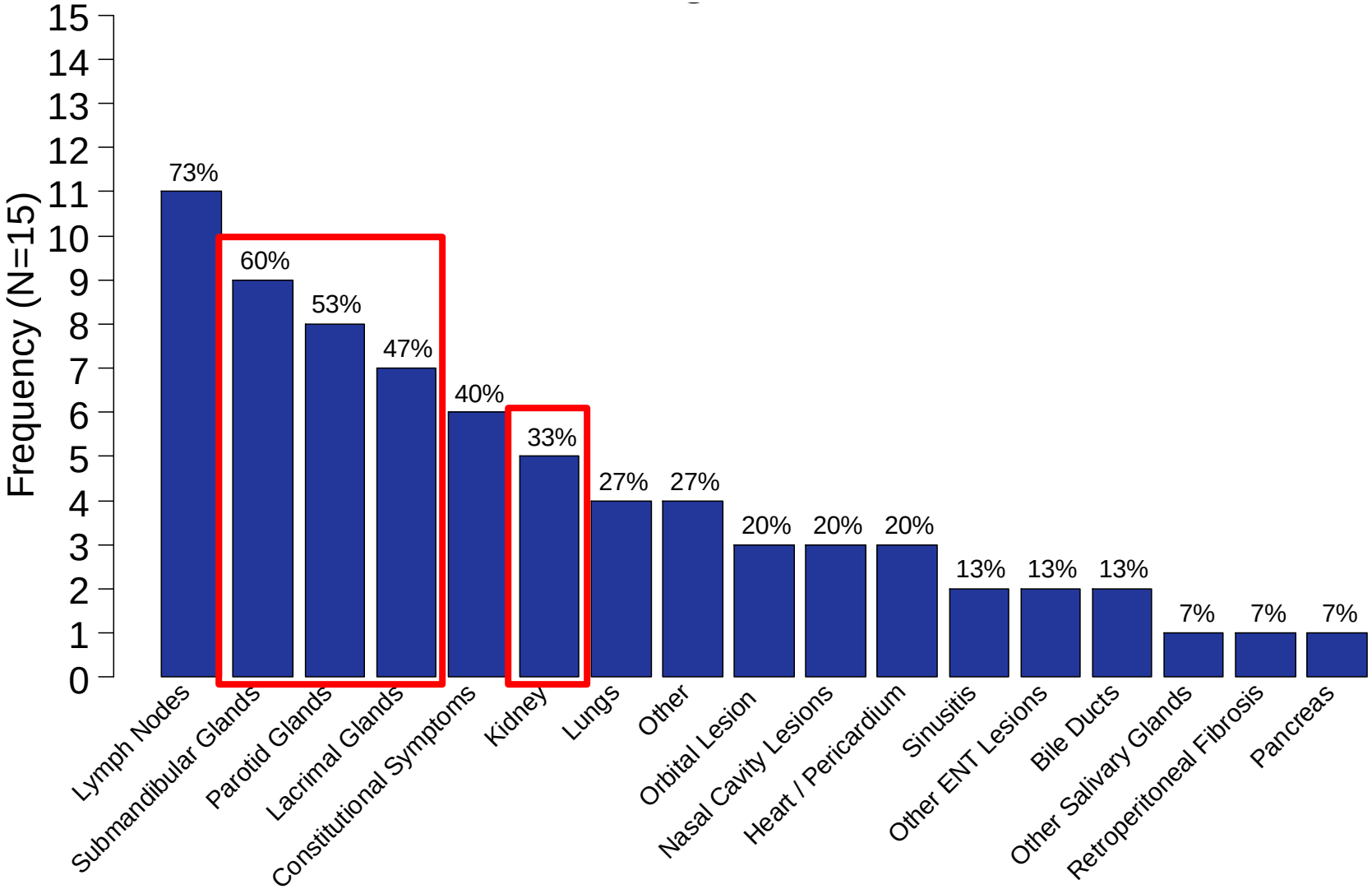
Baseline disease characteristics (N=15)

IgG4-RD Responder Index – median (range)	12 (2 - 30)
IgG4 level (normal < 86.4 mg/dl) – median (range)	220 (25 - 2415)
Previously treated – n	10

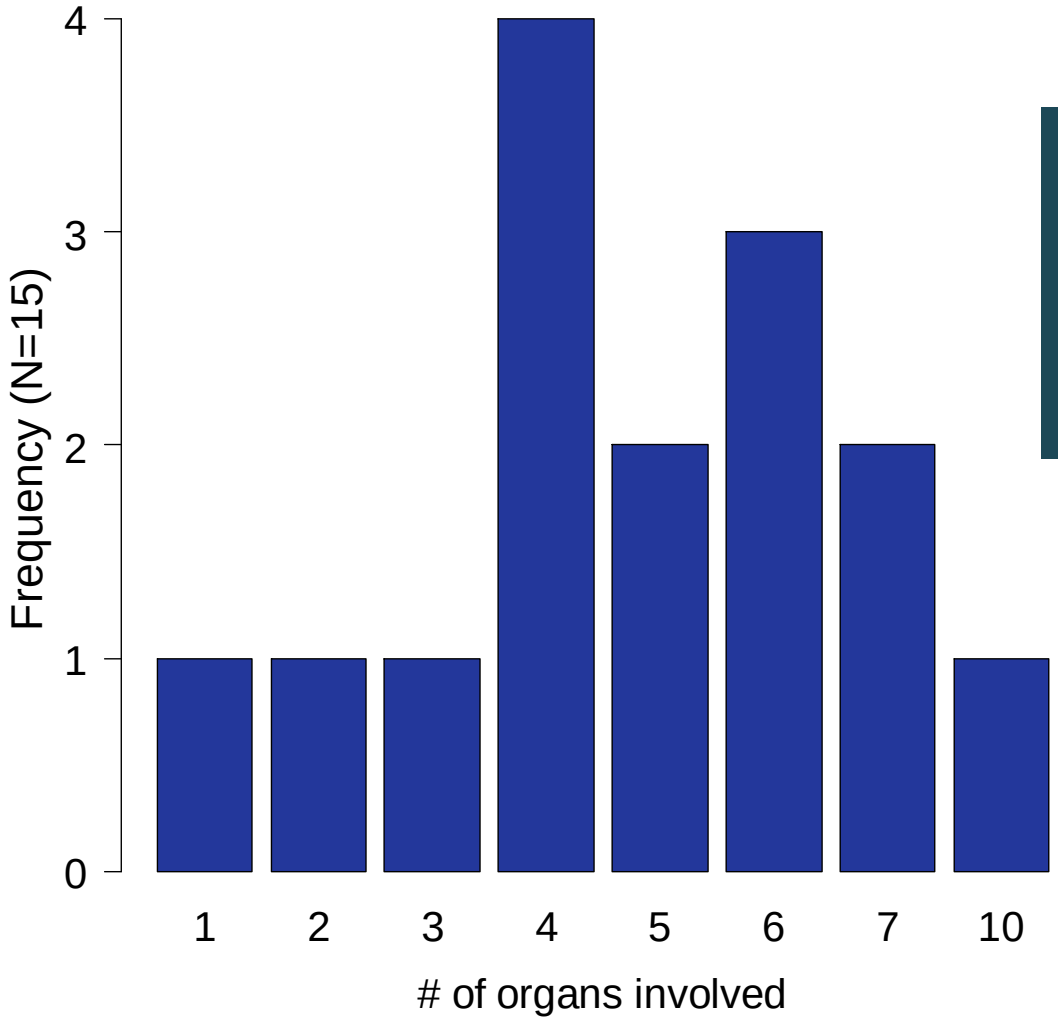
Previous Therapy (10 patients)

	Prednisone	Rituximab	Mycophenolate	Methotrexate
Prior	7	4	2	1
Most recent	5	3	2	0

Active Organs At Baseline



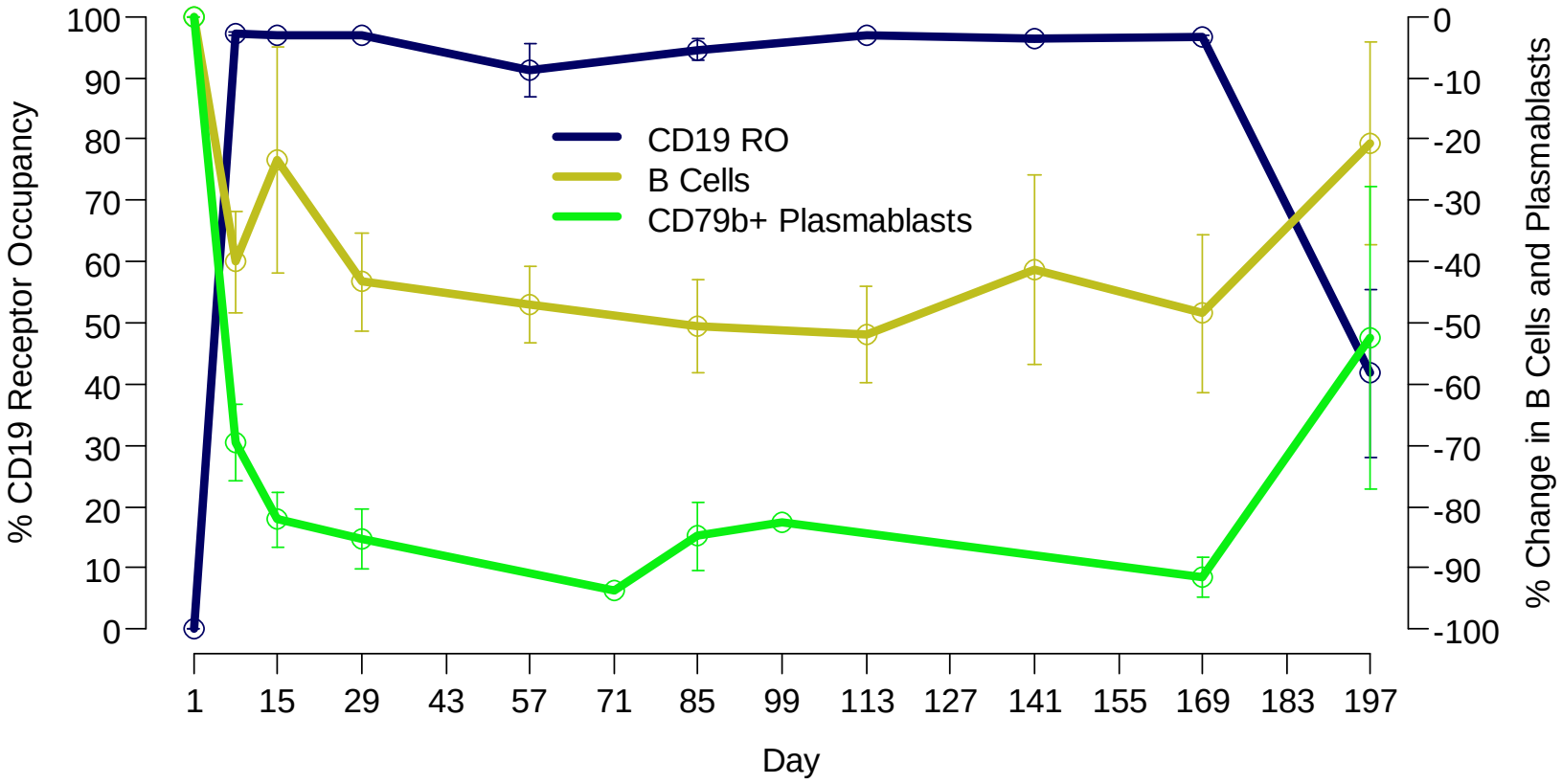
Number of Organs Involved At Baseline



13 patients had at least three organs involved

Median (Range)	**5 (1-10)**

Pharmacodynamics: Plasmablasts (CD79b+) and B Cells



CD19 receptor occupancy was maintained throughout the treatment period.

B cells decreased about 40 – 55% from baseline.

Plasmablasts decreased by about 70 – 80%.

Treatment Emergent Adverse Events (TEAEs): SUMMARY

13 patients (87%: 11 mild, 1 moderate, 1 severe).

Mild XmAb5871-03 TEAEs in > 1 Patient		
TEAE	All TEAE	Related TEAE*
MedDRA preferred term	Number (%)	Number (%)
Abdominal Pain	3 (20%)	2 (13%)
Diarrhea	2 (13%)	2 (13%)
Nausea	2 (13%)	2 (13%)
Chills	2 (13%)	2 (13%)
Headache	2 (13%)	2 (13%)

* Related is possibly, probably or definitely related to drug as per the investigator.

One patient developed a self-limited rash and arthritis after her 5th infusion (Day 57). Anti-drug antibodies positive, consistent with hypersensitivity reaction.

Two SAEs were reported in one patient, pneumonia and a recurrence due to non-compliance. Neither was considered related to XmAb5871.

Efficacy

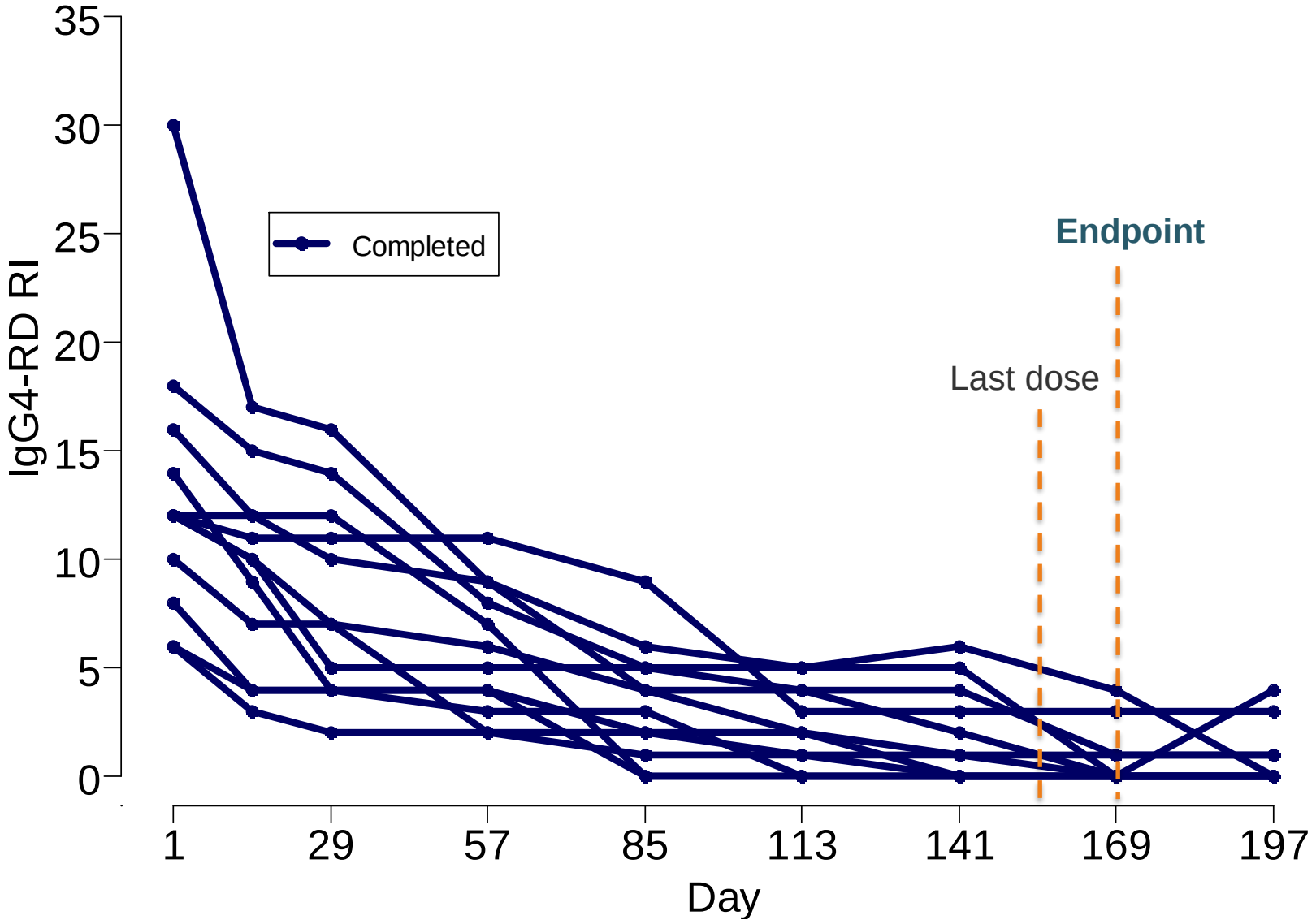
- 14 of 15 patients (93%) achieved a decrease of a least 5 points or more at some time in the study.
- 12 patients (80%) met the primary endpoint of at least a 2 point RI decrease at Day 169.
  - **8 of these 12 patients achieved remission at Day 169 defined as an IgG4-RD RI of 0 and no corticosteroids after month 2.**
  - **The other 4 patients achieved IgG4-RD RI scores of ≤ 4 at Day 169 and no corticosteroids after month 2 (all organs improved).**
- All 5 patients on corticosteroids at time of first XmAb5871 dose were tapered off in 2 months.

- One responded (RI 8 → 2) but discontinued at Day 57 (hypersensitivity).

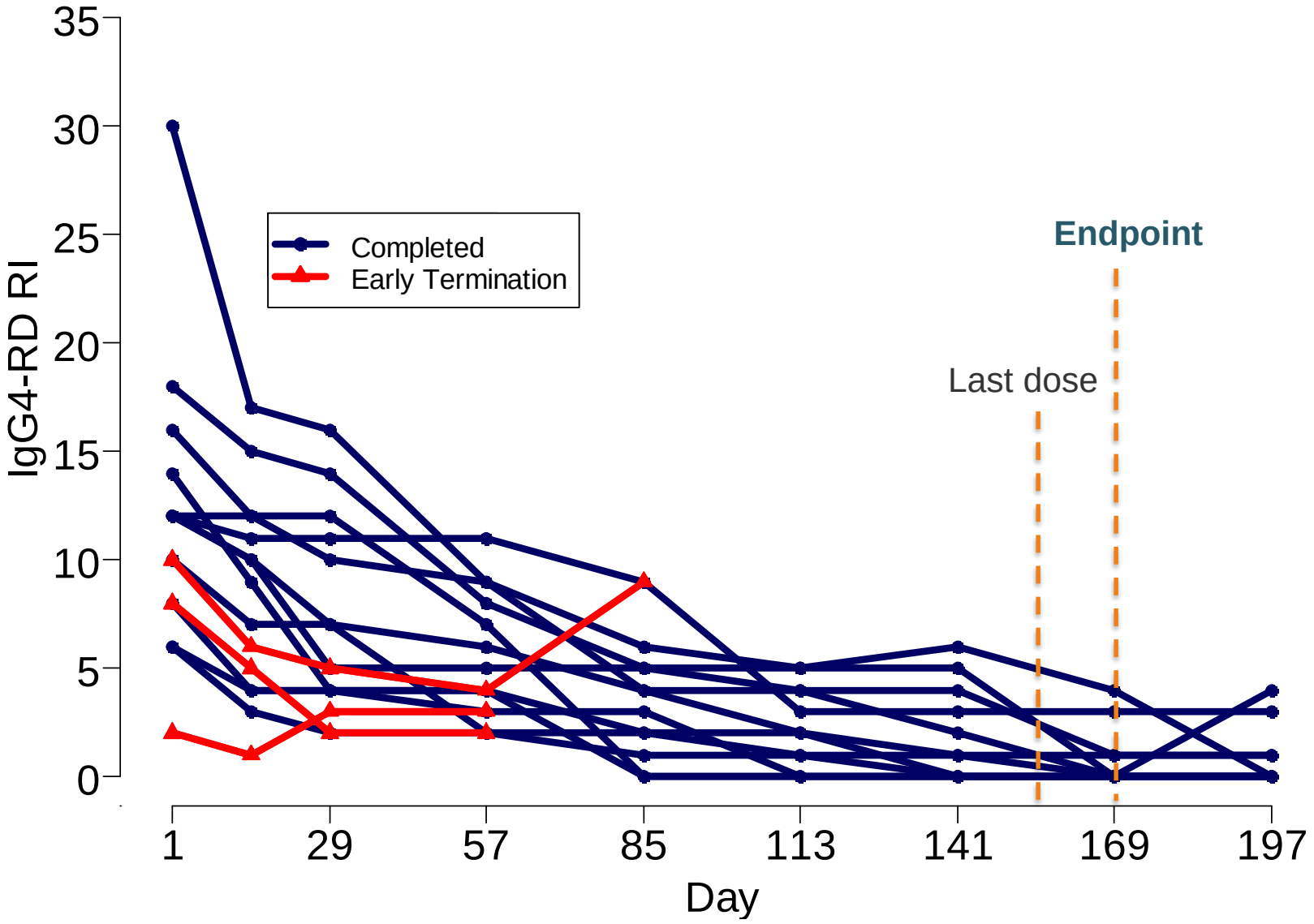
- One atypical presentation (single organ, larynx) did not respond after 6 doses. She failed subsequent rituximab therapy, and required surgery.

- One responded to XmAb5871 initially (RI 10 → 4) but lost response on Day 85. She failed to have a good response from subsequent rituximab therapy.

IgG4-RD Responder Index Over Time
For the 12 Subjects Completing the Trial



IgG4-RD Responder Index of Three Early Terminations



Conclusions

- XmAb5871 in active IgG4-RD was well tolerated. The most frequent AEs were GI Infusion-related symptoms.
- 12 patients (80%) completed the study. All 12 achieved the primary endpoint of a decrease of IgG4-RD RI of ≥ 2 at Day 169.
- Remission (IgG4-RD RI of 0 and no corticosteroids after month 2) was attained in 8 patients at Day 169; 4 others achieved an RI ≤ 4.
- Corticosteroids were tapered and discontinued in all five patients that were on corticosteroids at first XmAb5871 dose.
- Response to therapy occurred quickly, most within two weeks.
- Plasmablasts decreased by about 70-80%, B cells by 40-55%.
- XmAb5871 shows promising activity in IgG4-RD.

Thank you!

We thank the patients participating in this trial.