Treatment With Rilzabrutinib Results in Rapid and Significant Decrease in Steroid Use and Improved Quality of Life in Patients With Chronic Relapsing Pemphigus: BELIEVE Phase 2 Study (Part A)

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Disclosures

- Boards/officer of public or academic organization
  - Chair, Department of Dermatology, St George Hospital, Sydney, Australia
  - Professor of Dermatology, UNSW, Australia
- Dermatology society involvement: EADV International Board member, ISD Board of Directors, and President of ASDR
- Director, Premier Specialists: Clinical Trials Centre for Dermatology
- Inventor/Co-inventor of the PDAI, ABQOL and TABQOL measures
- Advisory board and principal investigator/investigator roles for Principia Biopharma and Roche
- Investigator/advisor supported by AbbVie, Amgen, ArgenX, AstraZeneca, Botanix, Dermira, Eli Lilly, Galderma, Janssen, Leo, Lilly, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB
- Patent for EB with topical sirolimus

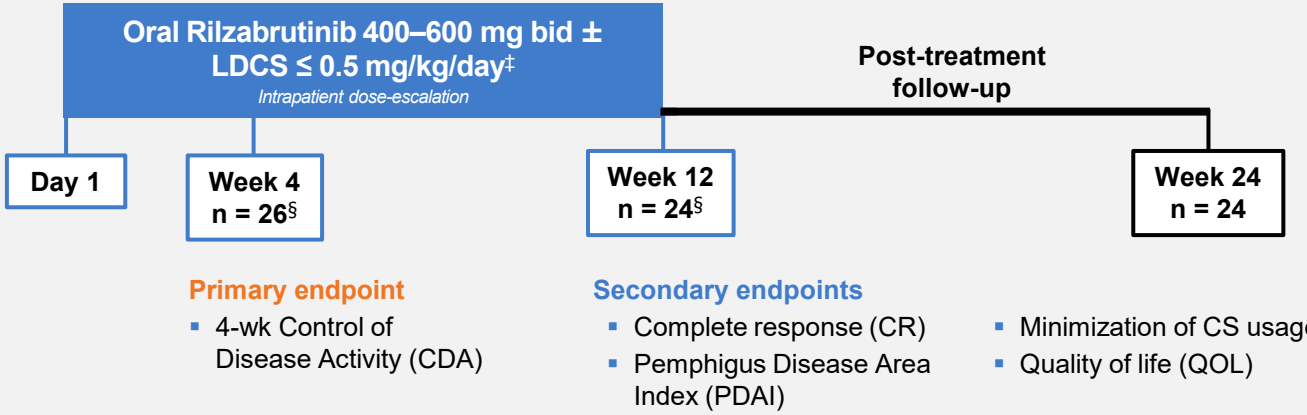
Newly Diagnosed and Relapsing Pemphigus Vulgaris Patients Were Treated With Oral Bruton Tyrosine Kinase (BTK) Inhibitor Rilzabrutinib

Rationale for BTK inhibition in pemphigus: BELIEVE phase 2 study

- BTK has broad role in rapid innate and delayed adaptive immune responses in pemphigus[1]
- Rilzabrutinib is potent, oral, and reversible BTK inhibitor[2]
- BELIEVE is an open-label, proof-of-concept phase 2 study of rilzabrutinib ± concomitant low-dose corticosteroids (LDCS)
  - Part A results are presented here (12 wk treatment; 12 wk follow-up)

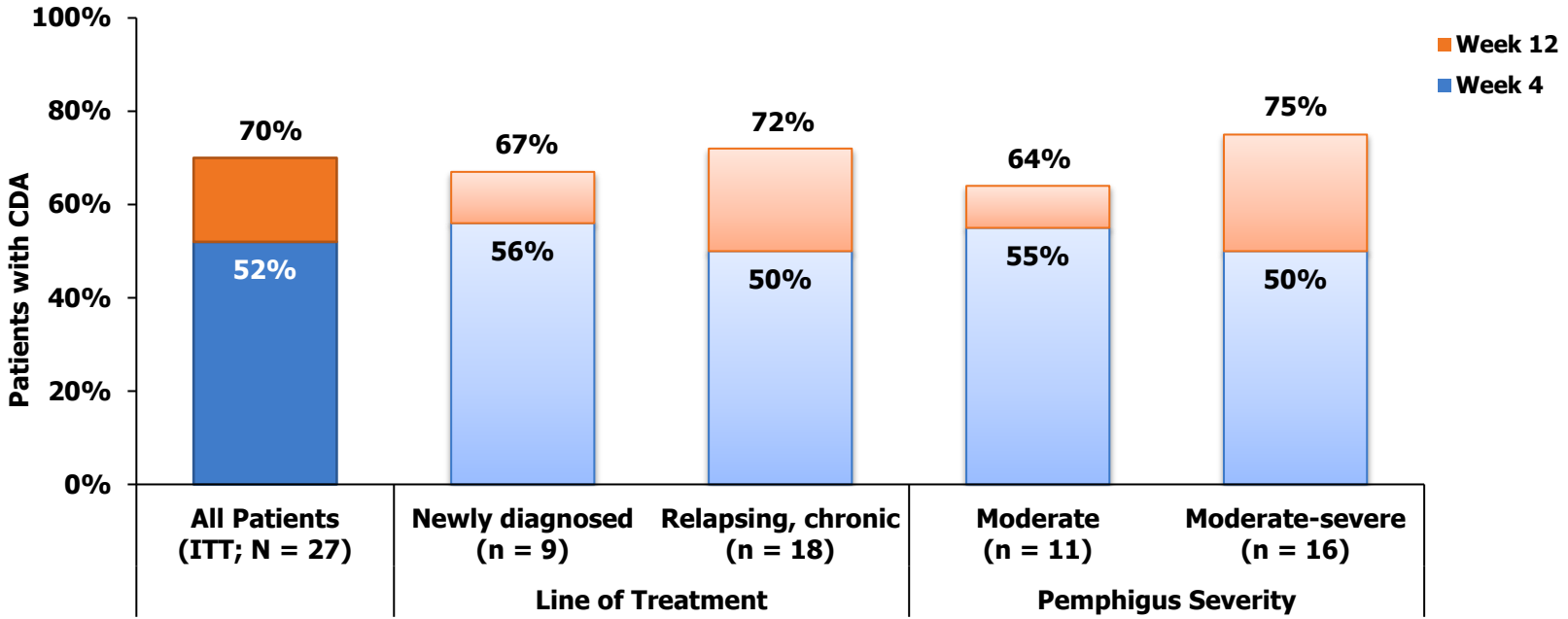
Part A PV patients (N = 27)

- Median age = 51 y
- 41% moderate and 59% moderate-to-severe PV*
- 33% newly diagnosed and 67% relapsing†
- Mean time from diagnosis for relapsing patients = 8.9 y (range, 1.1-25.3)



NCT02704429. 1. Didona D, et al. *Front Immunol.* 2019;10:1418. 2. Bradshaw JM, et al. *Nat Chem Biol.* 2015;11:525-531.
*Pemphigus severity: moderate (PDAI 8 to <15); moderate-to-severe (PDAI ≥ 15) per Shimizu T, et al. *J Dermatol.* 2014;41:969-973.
†Newly diagnosed ≤6 mo and relapsing >6 mo to 10 y from disease onset/diagnosis at screening.
‡Prednisolone or equivalent. §3 patients discontinued due to TEAEs unrelated to rilzabrutinib at days 10, 43, and 44.

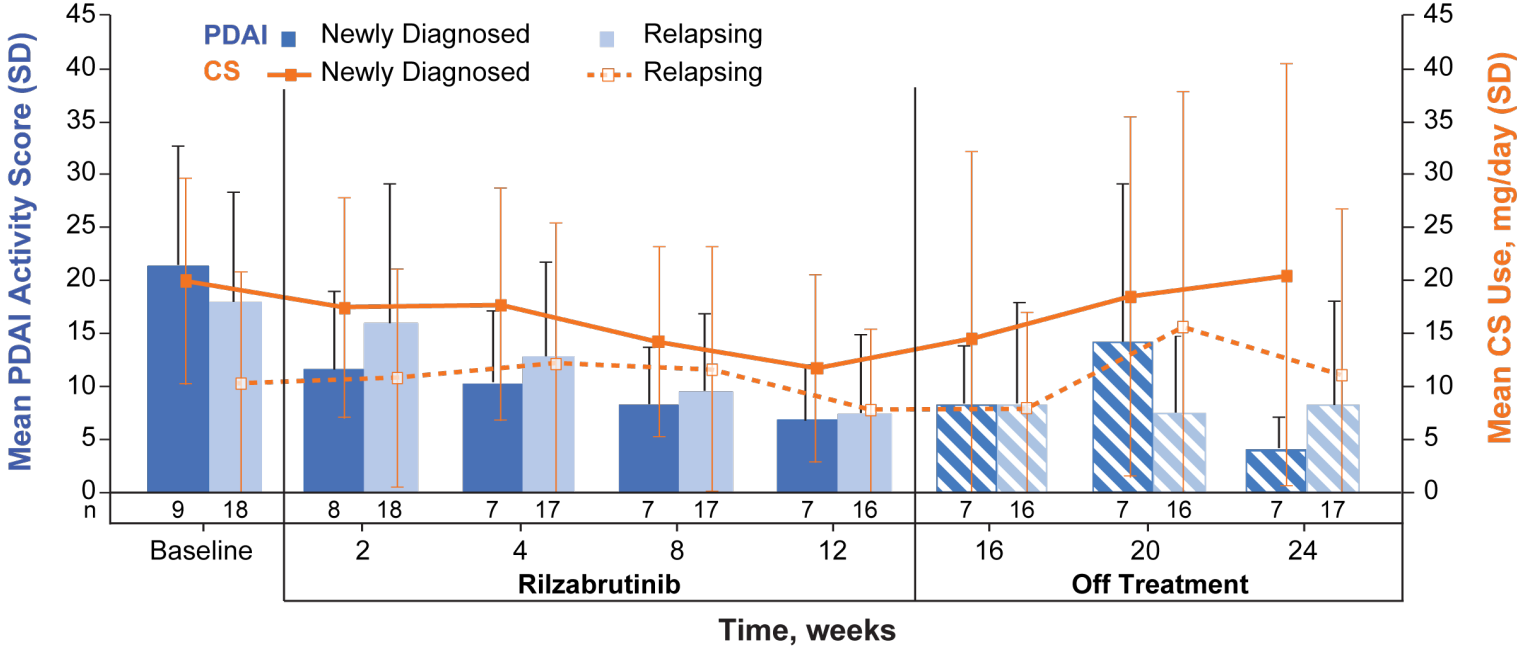
CDA Rates Were Consistently Improved Over Time Irrespective of Pemphigus History or Severity



- Control of Disease Activity (CDA) rates were consistently improved over time and similar based on treatment history* and pemphigus severity†
- Complete response was met in 6 (22%) patients, 4 by week 12 and additional 2 by week 20

*Newly diagnosed ≤6 mo and relapsing >6 mo to 10 y from disease onset/diagnosis at screening.
†Pemphigus severity: moderate (PDAI 8 to <15); moderate-to-severe (PDAI ≥ 15).

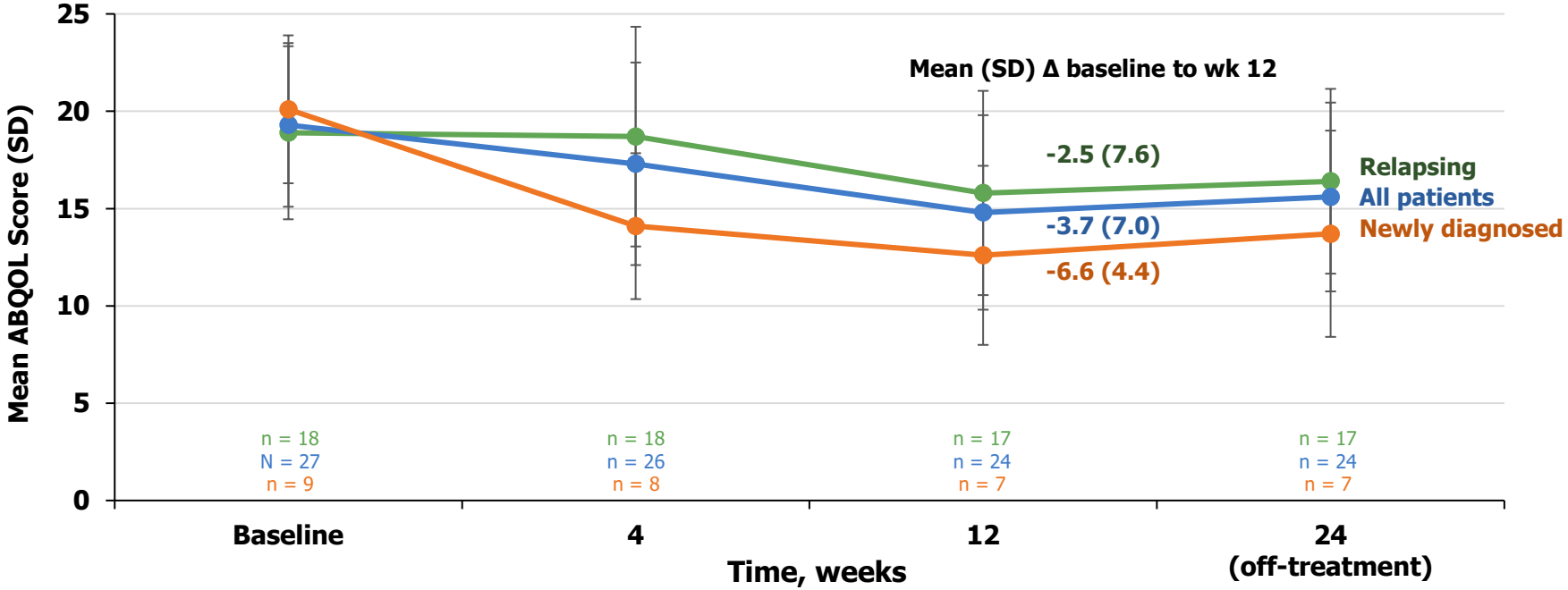
PDAI Activity Scores Were Improved and Accompanied by Reduced CS Use in Relapsing and Newly Diagnosed Patients



- From baseline to week 12, mean PDAI severity scores decreased in newly diagnosed and relapsing patients*
- Improved PDAI scores were accompanied by decreased mean CS use

*Newly diagnosed ≤6 mo and relapsing >6 mo to 10 y from disease onset/diagnosis at screening.

Mean ABQOL Scores Were Improved From Baseline to Week 12



- Changes from baseline through 12 weeks of treatment showed clinically-meaningful (~3 points) improved ABQOL scores in newly diagnosed and relapsing patients[1]*
- Improved ABQOL scores provide a reliable indicator of reduced disease severity, consistent with other responsiveness studies[2,3]

1. Sebaratnam DF, et al. *JAMA Dermatol.* 2013;149:1186-1191. 2. Patsatsi A, et al. *Acta Derm Venereol.* 2017;97:1145-1147. 3. Ferries L, et al. *Br J Dermatol.* 2020;183:944-945.
*Newly diagnosed ≤6 mo and relapsing >6 mo to 10 y from disease onset/diagnosis at screening.

Treatment-Related, TEAEs Were Mild-Moderate and Transient

Related TEAEs ≥ 10% (N = 27), n (%)	Grade 1	Grade 2	Grade 3
All AEs	9 (33)	8 (30)	1 (4)
Nausea	4 (15)	0	0
Upper abdominal pain	0	3 (11)	0

- Oral rilzabrutinib was well-tolerated, with mainly grade 1/2 and transient TEAEs
- One patient had treatment-related grade 3 cellulitis (SAE) that resolved with treatment and the patient completed the study

SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Summary and Future Directions

Efficacy	• Rapid clinical benefit: 52% CDA at 4 weeks in all pemphigus patients • Improved disease severity as measured by PDAI scores • Reduced CS use over a short time • Similar outcomes in newly diagnosed and relapsing patients
Safety	• Transient and mild-moderate AEs • Overall favorable risk/benefit profile
QOL	• Improved quality of life as measured by ABQOL scores
Ongoing Trials	• BELIEVE phase 2 Parts A and B show consistent results • Supports ongoing phase 3 PEGASUS pivotal study (NCT03762265) - completed enrollment

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