

# Long-Term Outcomes of REAL-SPEED: A Multicenter Retrospective Study of Ramucirumab Plus Erlotinib in EGFR L858R-Mutated NSCLC

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## DISCUSSION AND CONCLUSION

### Key Findings

- Long-term outcomes with first-line ramucirumab plus erlotinib in this real-world *EGFR* L858R–mutated population were **generally consistent with those reported in RELAY**, with median PFS and OS of **17.8 and 52.7 months**, respectively.
- Median TTFs for ramucirumab (**10.3 months**) and erlotinib (**14.0 months**) were also similar to the respective treatment exposure durations reported in the RELAY Japanese population (**11.0 and 15.2 months**).
- Among patients without CNS metastases, median PFS and OS were **21.3 and 53.6 months**, respectively, broadly consistent with the outcomes reported in RELAY, which excluded patients with CNS metastases. In patients with CNS metastases, median PFS and OS were **15.9 and 37.1 months**, respectively.
- Median TD-TKI and PFS2 were **30.0 and 32.5 months**, respectively, and osimertinib was the most commonly used subsequent EGFR-TKI, highlighting the frequent use of **EGFR-TKI sequencing, including osimertinib**, in clinical practice.
- No new safety signals were identified.**

### Conclusion

In this multicenter retrospective study, long-term outcomes with first-line ramucirumab plus erlotinib in patients with *EGFR* L858R–mutated NSCLC were generally consistent with those reported in RELAY. The prolonged TD-TKI and PFS2, together with the frequent use of subsequent EGFR-TKIs, including osimertinib, suggest that EGFR-TKI sequencing may be relevant to long-term disease management in this population.

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#### DISCLOSURES

NM received personal fees as honoraria from AstraZeneca, MSD, Chugai Pharmaceutical, Ono Pharmaceutical, Boehringer Ingelheim, Taiho Pharmaceutical, Novartis and Bristol Myers Squibb. MI received personal fees as honoraria from AstraZeneca, Eli Lilly Japan, Chugai Pharmaceutical, Taiho Pharmaceutical and Daiichi Sankyo. TS received personal fees as honoraria from AstraZeneca, Boehringer Ingelheim, Ono Pharmaceutical and Sanofi. YO received personal fees as honoraria from AstraZeneca, Eli Lilly and Chugai Pharmaceutical. HK received personal fees as honoraria from AstraZeneca. MT received grants and personal fees from AstraZeneca, Chugai Pharmaceutical, Eli Lilly Japan, and personal fees as honoraria from Ono Pharmaceutical, Bristol-Myers Squibb, Chugai Pharmaceutical, AstraZeneca, MSD, Novartis pharmaceuticals, Takeda Pharmaceutical, Taiho Pharmaceutical, Nippon Boehringer Ingelheim, Daiichi Sankyo, Pfizer Japan, Janssen Pharmaceutical. AT received grants from AstraZeneca, Daiichi-Sankyo, Taiho Pharmaceutical and Beigene, and personal fees as honoraria from Eli Lilly, Ono Pharmaceutical, Chugai Pharmaceutical, Bristol-Myers Squibb and MSD. KK received grants and personal fees as honoraria from AstraZeneca, and personal fees as honoraria from Ono Pharmaceutical, Chugai Pharmaceutical and Bristol-Myers Squibb. KI received grants and personal fees as honoraria from Ono Pharmaceutical and MSD, and personal fees as honoraria from Chugai Pharmaceutical and Eli Lilly. KO received personal fees as honoraria from AstraZeneca and GlaxoSmithKline. SI received grants from Chugai Pharmaceutical, and personal fees as honoraria from AstraZeneca. AH received personal fees as honoraria from AstraZeneca, MSD, Chugai Pharmaceutical, Taiho Pharmaceutical, Pfizer and Eli Lilly. KH received personal fees as honoraria from AstraZeneca. NS received grants and personal fees as honoraria from Eli Lilly, Ono Pharmaceutical, Boehringer Ingelheim, Taiho Pharmaceutical, Chugai Pharmaceutical, Takeda Pharmaceutical, Nippon Kayaku, Pfizer and Daiichi Sankyo, grants from Eisai and Shionogi, and personal fees as honoraria from AstraZeneca, MSD, Bristol Myers Squibb, Novartis and Kyowa Kirin. No potential conflicts of interest were disclosed by the other authors.

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## BACKGROUNDS

- Patients with *EGFR* L858R–mutated NSCLC generally have less favorable outcomes with EGFR TKIs than those with exon 19 deletion.
- In RELAY, ramucirumab plus erlotinib demonstrated a median progression-free survival (PFS) of 19.4 months and a median overall survival (OS) of 51.6 months in patients with L858R-mutated NSCLC. However, patients with central nervous system (CNS) metastases were excluded, and long-term real-world data remain limited.
- The REAL-SPEED study, **R**amucirumab plus **E**rlotinib for **A**dvanced non-small cell lung cancer harboring *EGFR* **L**858R mutation: A multicenter retro**S**pective obs**E**rvational cohort stu**D**y in Japan , previously reported real-world outcomes; here, we report long-term follow-up, including survival and subsequent treatment patterns.

## RESULTS

- A total of 168 pts were enrolled from 47 institutions in Japan.
- Median duration of follow-up time was 45.4 months.

| Table 1. Baseline characteristics |            |  |
|-----------------------------------|------------|--|
|                                   | N=168      |  |
| Median Age, years (range)         | 72 (37-87) |  |
| ≥65 , n (%)                       | 128 (76)   |  |
| ≥75, n (%)                        | 50 (30)    |  |
| Sex, n (%)                        |            |  |
| Male                              | 60 (36)    |  |
| Female                            | 108 (64)   |  |
| ECOG PS, n (%)                    |            |  |
| 0                                 | 76 (45)    |  |
| 1                                 | 86 (51)    |  |
| 2                                 | 6 (4)      |  |
| Smoking, n (%)                    |            |  |
| Ever                              | 57 (34)    |  |
| Never                             | 111 (66)   |  |
| CNS metastasis, n (%)             |            |  |
| Present*                          | 43 (26)    |  |
| Absent                            | 125 (74)   |  |

\* Among patients with CNS metastases, 15/43 (35%) received CNS-directed local therapy prior to systemic therapy.

### Patient characteristics

- Cases of central nervous system (CNS) metastasis accounted for 26% of the total cases.

| Table 2. Summary of first and second subsequent therapies |                    |    |
|-----------------------------------------------------------|--------------------|----|
|                                                           | Number of patients | %  |
| First subsequent line of therapy                          | 123                | 73 |
| Chemotherapy (excluding chemo-immunotherapy)              | 23/123             | 19 |
| EGFR-TKI                                                  | 86/123             | 70 |
| Erlotinib                                                 | 6/123              | 5  |
| Gefitinib                                                 | 1/123              | <1 |
| Afatinib                                                  | 6/123              | 5  |
| Osimertinib                                               | 73/123             | 59 |
| Immunotherapy (including chemo-immunotherapy)             | 14/123             | 11 |
| Second subsequent line of therapy                         | 66                 | 39 |
| Chemotherapy (excluding chemo-immunotherapy)              | 34/66              | 52 |
| EGFR-TKI                                                  | 20/66              | 30 |
| Erlotinib                                                 | 2/66               | 3  |
| Gefitinib                                                 | 1/66               | 2  |
| Afatinib                                                  | 6/66               | 9  |
| Osimertinib                                               | 7/66               | 11 |
| Immunotherapy (including chemo-immunotherapy)             | 12/66              | 18 |

### Subsequent therapies

- Subsequent therapies are summarized in **Table 2**. Among patients receiving first subsequent therapy, 70% received an EGFR-TKI, most commonly osimertinib (59%).

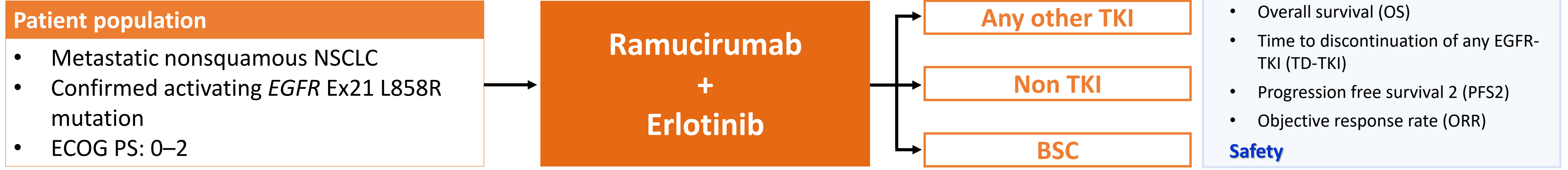
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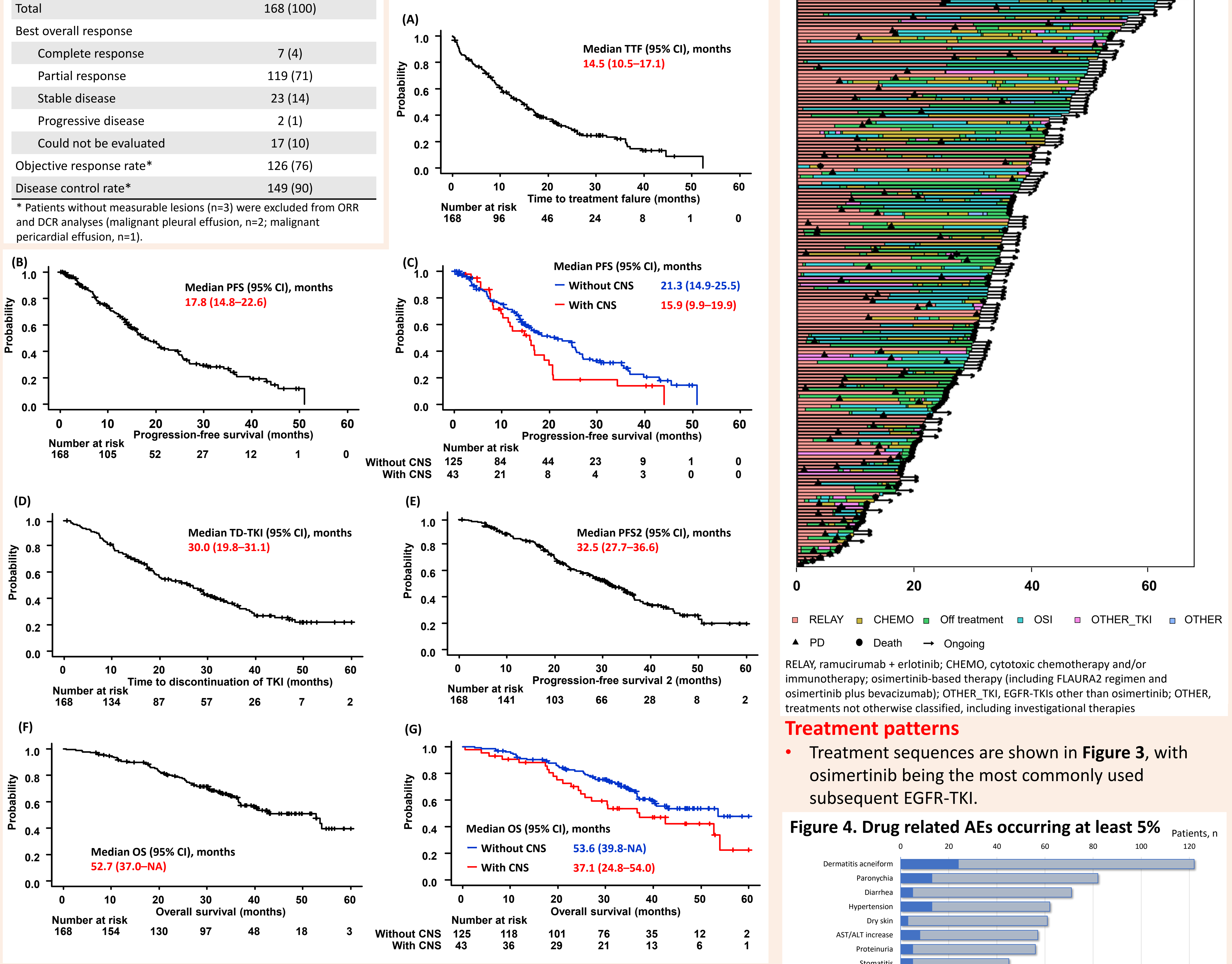
## METHODS

- REAL-SPEED was a multicenter, retrospective, observational study evaluating the real-world effectiveness and safety of first-line ramucirumab plus erlotinib in patients with metastatic *EGFR* L858R–mutated NSCLC (**Figure 1**).

**Figure 1. REAL-SPEED study design**



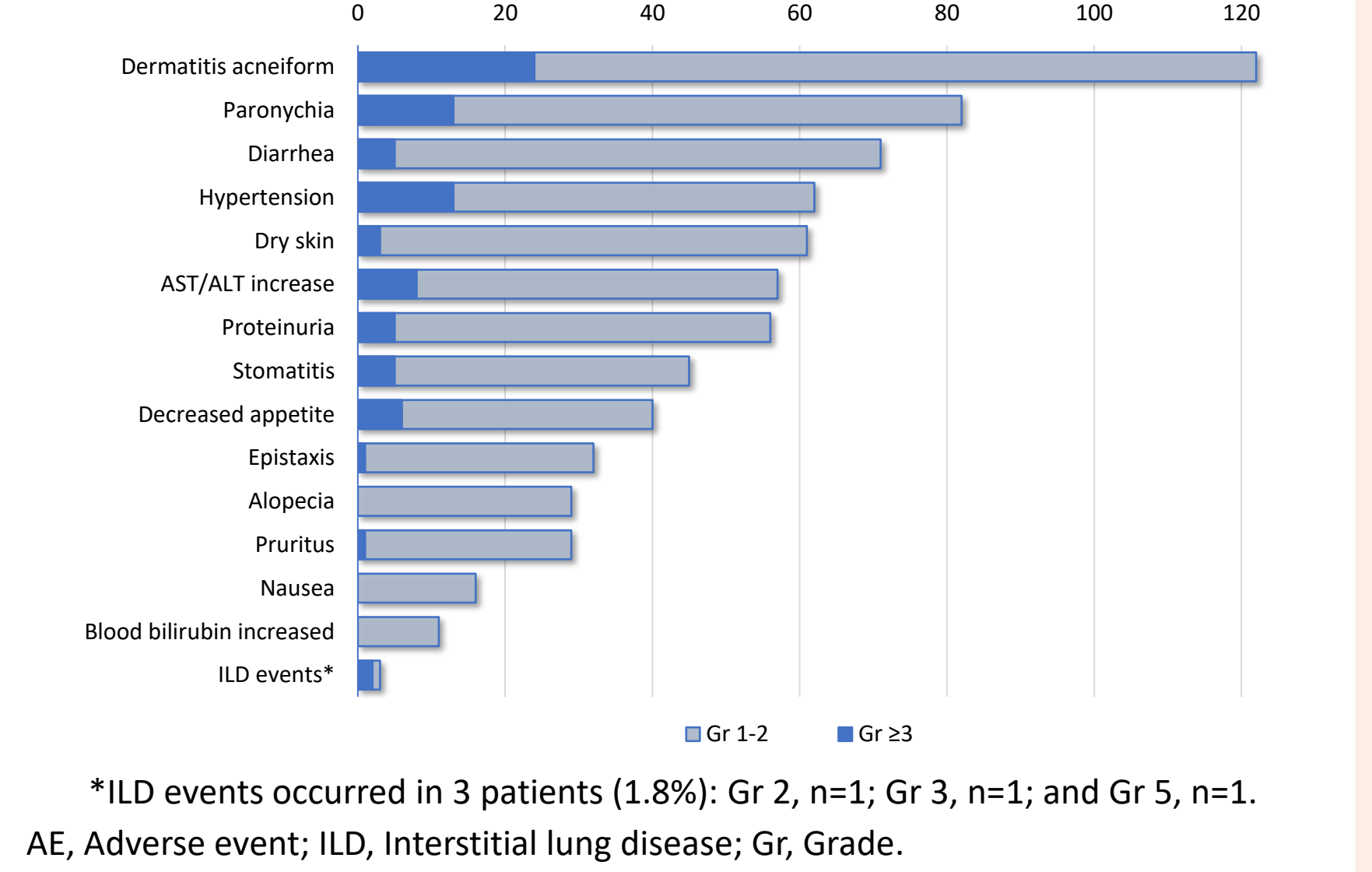
**Figure 2. Kaplan-Meier estimates of TTF (A), PFS (B–C), TD-TKI (D), PFS2 (E) and OS (F–G).**



### Treatment patterns

- Treatment sequences are shown in **Figure 3**, with osimertinib being the most commonly used subsequent EGFR-TKI.

**Figure 4. Drug related AEs occurring at least 5%**



### Safety

- AEs occurring in ≥5% of patients are shown in **Figure 4**, with dermatitis acneiform being the most common.



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