Methods

**EMPHASIS Study population:** Pts with locally advanced SqNSCLC (histologically or cytologically confirmed stage IIB not amenable to radical radiotherapy, or metastatic stage IV) failing first line platinum based doublet chemotherapy.

**Study design:** EMPHASIS explores the differential activity of second line E vs D on PFS in SqNSCLC. The expected hazard ratio (HR) of E vs D was 0.765 for the PFS (median PFS: E, 4.0 and D: 2.7 months (mo); and 1.23 for the PFS (median PFS: E: 2.2 mo and D: 1.6 mo). A sample size of 500 pts was needed to achieve 85% power for testing the expected hazard ratio of 1.82 at a two-sided α level of 0.05.

**Randomization:** Block stratified by center (minimalisation algorithm (5))

**Strata:**

- **Primary endpoint:** PFS
- **Secondary endpoints:** OS, Objective Response, Disease Control

**Primary end-point:** PFS

**Randomization:** Block stratified by center (minimalisation algorithm (5))

**Strata:**

- E: 150 mg p.o. daily or D: 75 mg/m² i.v. on day 1 of each 21-day cycle

**PROSE squamous cohort**

The SqNSCLC pts used in the combined analysis are a subgroup of the study population of pts with histologically or cytologically confirmed, second-line, locally advanced squamous NSCLC. The primary endpoint in PROSE was OS with PFS as a secondary endpoint and pts were randomized to receive second-line E (150 mg p.o. daily) versus chemotherapy (up to 6 cycles of 75 mg/m² i.v. or premedicated 500 mg i.v. every 21 days). A minimalisation algorithm with stratification on VS, PS, smoking, and center was used in the randomization.

**Results**

**Figure 1**

**Figure 2**

**Figure 3**

**Summary and Conclusions**

The final analysis of EMPHASIS did not show a differential activity on PFS of E vs D in SqNSCLC pts stratified by VS status. These results are at variance with trial assumptions and previous studies. A possible explanation is the lack of OS benefit within the closure of the study. VSP patients had a better OS than VSP, but no effect of treatment was found on either PFS or OS.

For the combined cohort of EMPHASIS and PROSE-Sq pts, pts in E have a significantly higher risk of progression (and marginally significant for death) compared to D, for both VSP and VSP patients, while pts with a history of lower risk of progression and death compared to VSP.

**References**