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Presentation Title: SATURN: A Double-Blind, Randomized, Phase III Study of Maintenance Erlotinib versus Placebo Following Non-Progression with 1st-Line Platinum-Based Chemotherapy in Patients with Advanced NSCLC.

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Background and Objectives

Recent trials of maintenance therapy immediately after first-line therapy in patients with NSCLC have reported improvements in progression-free survival (PFS). In the TALENT trial of first-line therapy with erlotinib with concurrent chemotherapy, there was a trend towards increased time to progression or death in patients who continued erlotinib after 6 cycles of chemotherapy. The SATURN trial, presented by Dr. Federico Cappuzzo (Istituto Clinico Humanitas IRCCS, Rozzano (Milan), Italy), was initiated to determine if erlotinib therapy immediately following first-line chemotherapy would delay disease progression.

Methods and Subjects

Chemotherapy-naïve patients with advanced NSCLC (N=1,949) received first-line therapy with 4 cycles of a platinum-based doublet. Patients without progressive disease after initial therapy (N=889) were randomized to either erlotinib (150 mg/day) (N=438) or placebo (N=451). The co-primary endpoints were PFS in all patients and PFS in patients with epidermal growth factor receptor (EGFR)-positive tumors by IHC. The secondary endpoints were overall survival (OS) in all patients and in those with EGFR-positive tumors; OS and PFS in patients with EGFR-negative tumors; biomarker analyses; safety; time to symptom progression; and quality of life (QoL).

Baseline characteristics were balanced in both arms. The median age was 60 years and 74% of patients were male. Fewer than 1% of patients in both arms had a complete response (CR) to first-line therapy, 42% in the erlotinib arm versus 47% in the placebo arm had a partial response (PR), and 58% in the erlotinib arm versus 52% in the placebo arm had stable disease (SD).

Results and Conclusions

In the intent-to-treat (ITT) population, the median PFS was 12.3 weeks in the erlotinib arm (N=437) versus 11.1 weeks in the placebo arm (N=447). The 12- and 24-week PFS rates were, respectively, 53% and 31% in the erlotinib arm versus 40% and 17% in the placebo arm (HR=0.71, $p<0.0001$) (Figure 1). In patients with EGFR-positive tumors, the 12- and 24-week PFS rates were, respectively, 54% and 32% in the erlotinib arm (N=307) versus 40% and 18% in the placebo arm (N=311) (HR=0.69, $p<0.0001$).

The response rate (CR+PR) was 11.9% in the erlotinib arm versus 5.4% in the placebo arm ($p=0.0006$). The SD rate at ≥6 weeks was 48.6% in the erlotinib arm versus 45.4% in the placebo arm (NS). The disease control rate (CR+PR+SD) at ≥12 weeks was 40.8% in the erlotinib arm versus 27.4% in the placebo arm ($p<0.0001$).

Erlotinib improved PFS in all subgroups. Erlotinib improved PFS to a greater degree in patients with adenocarcinoma histology (HR=0.60, $p<0.0001$) than in those with squamous cell histology (HR=0.76, $p=0.0148$) (Figure 2).

Erlotinib improved PFS in patients with both EGFR wild-type tumors (HR=0.78, $p=0.0185$) and EGFR mutation-positive tumors (HR=0.10, $p<0.0001$) but by a much greater degree in those with EGFR mutations.

As expected, more patients in the erlotinib arm had rash (60% vs 9%) and diarrhea (20% vs 4%) (Figure 3). Withdrawal due to any adverse event (AE) was reported in 5% of erlotinib patients versus 2% of placebo patients.

Erlotinib maintenance therapy significantly improved PFS versus placebo. There was significant improvement in response and disease control with erlotinib therapy. The clinical benefit was achieved across the majority of patient subgroups, irrespective of histology, race, or smoking status. The safety profile was consistent with previous trials, with no new safety signals. The erlotinib arm had a low rate of discontinuation versus the placebo arm. There was no deterioration in QoL in patients treated with erlotinib versus those treated with placebo.

Questions and Answers

Question 1: Did you analyze the patients' *K-Ras* status?

Dr. Cappuzzo: We did analyze *K-Ras* status and those results will be presented in a session on June 1.

Question 2: When will the OS data be ready?

Dr. Cappuzzo: We should present these data in about the next month.

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Figure 1: PFS: All Patients (ITT) [DSCF6197.jpg]

Figure 2: PFS According to Histology [DSCF6209.jpg]

Figure 3: Summary of Safety Data [DSCF6216.jpg]