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Bortezomib + gemcitabine (Gem)/carboplatin (Carbo) results in encouraging survival in advanced non-small cell lung cancer (NSCLC): Results of a phase II Southwest Oncology Group (SWOG) trial (S0339).

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BACKGROUND

Bortezomib (PS-341), a small molecule proteasome inhibitor, has single agent activity in NSCLC and potentiates Gem/Carbo in pre-clinical models in a sequence-specific manner (Mortensen, Cancer Chem Pharm, 2004). A phase I trial of Gem/Carbo + PS-341 in patients (pts) with advanced NSCLC yielded an encouraging response rate of 48%. Here we describe the results of a SWOG phase II study of this regimen in advanced NSCLC.

METHODS

114 eligible chemonaive stage IV and selected stage IIIB (pleural effusion) NSCLC pts received Gem 1000 mg/m² on days 1, 8 and Carbo AUC 5 on day 1, followed 1 hour later by PS-341 1.0 mg/m² on days 1, 4, 8, 11, with cycles repeated every 3 weeks. Non-progressing pts could continue PS-341 alone after 4 cycles.

RESULTS

Pt characteristics: Median age: 64 years; Sex M/F = 68/46; Performance status

0/1 = 50/64; stage IIIB/IV = 13/101. Response rate: 20% (95% CI 13-29%); 66% (95% CI 56-75%) had stable disease. At a median follow-up of 13 months, progression free and median survival times were 5 months (95% CI 3.5-5.3) and 11 months (95% CI 8.2-12.5). One-year survival was 46% (95% C.I. 37-55%). Most common grade 3/4 toxicities: neutropenia (52%), thrombocytopenia (63%), and fatigue (13%). Ongoing correlative studies are examining markers of proteasome

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Intermittent chemotherapy in metastatic androgen-independent prostate cancer (AIPC): Initial results from ASCENT.

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BACKGROUND:

Phase III studies document a survival benefit for 10-12 cycles of docetaxel-containing chemotherapy in AIPC. Further management of patients who complete chemotherapy in response status remains ill-defined. Single-institution phase II data suggest that re-treatment with the same regimen after a treatment holiday is feasible in selected patients. This approach was prospectively tested in a multi-institutional trial.

METHODS:

ASCENT was a multi-institution randomized clinical trial designed to compare the activity and safety of weekly DN-101 (45 µg on day 1) plus docetaxel (36 mg/m² iv on day 2 for 3 weeks of a 4-week cycle) to placebo + docetaxel in patients with chemotherapy-naïve metastatic AIPC. ASCENT was the first large trial to prospectively evaluate intermittent chemotherapy. Patients could opt to suspend treatment if they had a

confirmed > 50% reduction in serum PSA and a serum PSA ≤ 4 ng/ml. PSA was monitored every 4 weeks (CT scans every 8 weeks in patients with measurable disease) during the treatment holiday. Treatment was resumed when serum PSA rose by ≥ 50% and was ≥ 2 ng/ml or for other evidence of disease progression. The study was not powered to compare treatment holiday outcomes between the two arms.

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