Objectives: To assess the response rate (RR), using RECIST criteria, patient safety, and time to progression (TTP), duration of response (DOR), and overall survival (OS) in patients (pts) with refractory (Ref) and sensitive (Sen) SCLC and advanced NSCLC treated with SNS-595.
Methods: In both studies, SNS-595 was given q21-days at a dose of 48 mg/m^2 IV bolus for up to 8 cycles. Both studies used a 2-stage Fleming design. The SCLC study had 2 strata, refractory (Ref = relapsed <90 days after end of initial therapy or never responded) and sensitive (Sen = relapse >90 days after response to initial therapy). The SCLC study was powered to distinguish between 4% and 18% RR for the Ref and 11% vs 30% RR for the Sen strata. The study enrolled 20 pts in stage 1 for both strata and required at least 1 response in the Ref and 2 responses in the Sen for continuation to stage 2 and enrollment of 20 more pts in each stratum.
The NSCLC study was powered to distinguish between an RR of disinterest of 3% and one of interest at 15%. The study required a minimum of 1 response in the first 25 pts for study continuation to study stage 2 with 25 more pts.
Results: See the table.

Patient demographics, outcomes, Gr 3 or 4 AEs (>10%).

# Eval	SCLC-Sen 11	SCLC-Ref 20	NSCLC 25
Age (yrs) (med, range)	56, 46−65	60, 46−81	60, 35−76
Sex (M/F)	6/9	11/6	16/9
Race (Cauc, Afr-Amer)	15/0	17/0	22/3
# cycles (median, range)	4, 2−5	2, 1−6	2, 2−6
Best response			
Complete resp (CR)	0	0	0
Partial resp (PR)	2	0	0
Stable dis (SD)	7	5	14
Progressive dis (PD)	2	15	11
# (%) Pts with Gr 3 or AEs	2 (14%)	9 (45%)	8 (32%)
Neutropenia	2	3	2
Febrile neutropenia	0	2	1
Pneumonia	0	2	3

Conclusions: SNS-595 demonstrates clinical activity as single agent 2nd-line therapy in SCLC-Sen and NSCLC. For SCLC-Sen pts, overall RR is 2/11 (18%), with 9/11 (82%) showing SD or better. For NSCLC pts, over 50% show SD. SNS-595 is well tolerated with neutropenia being the main Grade 3 or 4 AE that occurred in 8−18% of pts. SNS-595 met the pre-determined RR for 14 pts in the SCLC-Sen cohort warranting expansion of this cohort to additional patients. Further accrual and follow-up continues.

6548 POSTER

Phase II study of sunitinib malate (SU) as consolidation therapy in patients (pts) with locally-advanced or metastatic non-small cell lung cancer (NSCLC)

R. Gervais[1], J.D. Hainsworth[2], N. Blais[3], J.C. Soria[4], J. Laskin[5], J.T. Hamm[6], A. Lipton[7], L. Tye[8], R. Chao[8], R.D. Page[9]. [1]*Centre François Baclesse, Avenue du General Harris, Caen, France;* [2]*The Sarah Cannon Research Institute, Suite 110, Nashville, USA;* [3]*CHUM – Hôpital Notre-Dame, Hématologiste et Oncologue Médical, Montreal, Canada;* [4]*Institut Gustave Roussy, Rue Camille Desmoulins, Villejuif, France;* [5]*BC Cancer Agency, West 10th Avenue, Vancouver, Canada;* [6]*Norton Healthcare Inc., Louisville Oncology Clinical Research Program, Louisville, USA;* [7]*Penn State University, Penn State Milton S Hershey Medical Center, Hershey, USA;* [8]*Pfizer Inc, Global Research and Development, La Jolla, USA;* [9]*The Center for Cancer and Blood Disorders, West Magnolia Avenue, Fort Worth, USA*

Background: SU is an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET, and FLT3, approved for the treatment of advanced RCC and imatinib-resistant or -intolerant GIST. An earlier phase II study of sunitinib monotherapy in treatment-refractory NSCLC reported an 11.1% response rate. This study has been evaluating the activity of SU in NSCLC pts when used as consolidation therapy following standard first-line therapy.
Materials and Methods: Pts are treated with up to 4 cycles of carboplatin (AUC=6 mg·min/mL) plus paclitaxel (175–225 mg/m^2) (CP), followed by up to 9 cycles on study of SU (50 mg/d in 6-wk cycles: 4 wks on treatment, followed by 2 wks off) in this ongoing open-label, uncontrolled, multicenter, phase II trial. The efficacy and safety of single-agent SU following CP was assessed in adult pts with locally advanced or metastatic NSCLC, with no prior systemic or antiangiogenic therapy for NSCLC, ECOG PS 0/1, and adequate organ function. The primary endpoint is 1-year survival. Secondary endpoints include objective response rate, progression-free survival, overall survival, and safety measures.
Results: 84 pts have been enrolled (81 pts treated), and data on 76 pts are reported. Baseline characteristics have included: mean age 61 yrs (range 30–81); male 61%; ECOG PS 0/1/2 36%/63%/1%; smoker 89%; adenocarcinoma 36%, squamous cell carcinoma 21%, large cell carcinoma 21%, other 22%. Median number of CP cycles was 4 (range 1–4); median number of SU cycles was 2 (range 1–5+) with 52 pts starting 4 cycles of CP and 64 pts receiving at least 1 dose of sunitinib. At completion of CP, there were 13 PR, 44 SD and 9 PD as best response (n = 68). To date, of pts receiving SU, 1 initial PR became a CR, and 1 SD converted to PR. 92% of pts in the CP treatment phase and 89% in the consolidation phase experienced an adverse event (AE). The most common AEs in SU-treated pts were fatigue (38%), diarrhea (36%), nausea (23%), the majority of which were mild-to-moderate in severity. The most common grade 3/4 AE with SU was fatigue (13%/2%). 13 pts discontinued SU due to an AE.
Conclusions: SU is associated with acceptable safety when used following first-line carboplatin/paclitaxel therapy in adult pts with locally advanced or metastatic NSCLC. The preliminary confirmed response rate to CP of 19% (13/68) is similar to that expected for this pt population; additional tumor reduction may occur in some pts with early SU treatment following chemotherapy.

6549 POSTER

Treatment of recurrent or progressive brain metastases with patupilone in patients with non-small cell lung cancer (NSCLC): results of a multicenter, open-label phase II study

L. Abrey[1], A. Johri[2], P.Y. Wen[3], R. Govindan[4], H.J. Reimers[5], H.I. Robins[6], S. de Bedout[2], L. Hennan[2], J.L. Ko[2], J.R. Rigas[7]. [1]*Memorial Sloan-Kettering Cancer Center, Department of NeurologyC-725, New York, USA;* [2]*Novartis Pharmaceuticals Corporation, Oncology, East Hanover, USA;* [3]*Dana-Farber/Brigham and Women's Cancer Center, Oncology, Boston, USA;* [4]*Washington University School of Medicine, Oncology, St. Louis, USA;* [5]*Saint Louis University School of Medicine, Oncology, St. Louis, USA;* [6]*University of Wisconsin Hospital & Clinics, Oncology, Madison, USA;* [7]*Norris Cotton Cancer Center, Dartmouth Medical School, Lebanon, USA*

Background: Advances in chemotherapy and delivery of radiation therapy have improved overall survival for patients with advanced non-small cell lung cancer (NSCLC); however, central nervous system (CNS) metastases occur in ⩾50% of patients with NSCLC and limits the survival benefits of current therapies. The novel epothilone patupilone has shown antitumor activity, in contrast to taxanes, in preclinical brain tumor models and in patients with NSCLC. The current study evaluated the activity of patupilone for the treatment of recurrent or progressive brain metastases in patients with NSCLC. All of these patients progressed after previous chemotherapy, surgery, and/or radiation to the brain.
Material and Methods: This was an open-label, multicenter, phase II, single-arm, multinomial, 2-stage study (25 patients per stage). Patients had histologically confirmed NSCLC and ⩾1 recurrent, bidimensionally measurable intracranial lesion ⩾2 cm. Patupilone was administered as a 10 mg/m^2 single IV infusion over 20 minutes every 3 weeks until disease progression (PD), satisfactory response, or unacceptable toxicity. Safety was assessed by adverse event (AE) reporting. Early progression (PD or death before cycle 1, day 21) and response rate (alive without PD at cycle 4, day 1) were the primary efficacy endpoints.
Results: The clinical review of emerging data consisted of 15 patients with a median age of 59 years (range, 40 to 67 years). The most commonly reported AEs related to the study drug were National Cancer Institute Common Toxicity Criteria grade 1/2 diarrhea (7/15 patients; 47%), nausea (4/15 patients; 27%), and fatigue (3/15 patients; 20%). There were 6 grade 3 AEs reported: 4 events related to study drug (3 cases of diarrhea, 1 additional case of diarrhea and neutropenia) and 2 events not related to study drug (confusion, dementia). There were 3 grade 4 AEs reported but not related to study drug (colitis, pulmonary embolism, headache). Five (33%) patients experienced early progression and 6 (40%) patients responded to therapy (without progression by cycle 4, day 1) for a median of 8 cycles (range, 5 to 13 cycles). The remaining 4 patients had stable disease or have not reached cycle 4 at the time of the clinical review.
Conclusions: Patupilone was well tolerated and has shown activity in patients with CNS metastases from advanced NSCLC. Further studies warrant investigation of patupilone as a treatment for brain metastases from NSCLC.