Supplementary Table 1: Summary of eligibility criteria

Sex and age	• Males or females, ≥ 18 years of age
Histological diagnosis	• Histological diagnosis of NSCLC which, in the openison of the local pathologist and the treating physician, was of non-squamous histology. Patients were enrolled based on local diagnosis; an independent centralized pathological review was performed on all enrolled patients.
Tumor stage	• Stage IIIB (with pleural effusion and/or positive supraclavicular lymph nodes) or stage IV prior to induction therapy
Biopsy specimen	• An adequate tumor biopsy specimen had to be available for TS assessment. The local diagnostic slides, pathology report and tissue material had to be available for central review.
Health status	• ECOG performance status 0 or 1 • Estimated life expectancy ≥ 12 weeks
Bone marrow reserve	• ANC ≥ 1.5 x 10^9/L • Platelets ≥ 100 x 10^9/L • Hemoglobin ≥ 9 g/dL
Hepatic function	• Bilirubin ≤ 1.5 x ULN • Hepatic enzymes ≤ 3.0 x ULN (< 5 x ULN acceptable if liver had tumor involvement)
Renal function	• Creatinine clearance ≥ 45 mL/min
Previous treatment	• Previous systemic treatment for lung cancer not allowed, except for previous palliative radiotherapy to non-target metastatic lesions (to < 25% of the bone marrow) and surgery.
Tumor assessment	• At least 1 unidimensionally measurable lesion meeting RECIST criteria, and adequate tumor biopsy specimen had to be available for TS assessment.

Exclusion criteria	• Small cell, large cell neuroendocrine or carcinoid histology, squamous cell carcinoma or tumors with a predominatly squamous component • Serious uncontrolled medical condition that would compromise the patient's ability to adhere to the protocol • Second primary malignancy • Central nervous system metastases • Concurrent administration of any other systemic antitumor therapy, including adjuvant chemotherapy • Clinically detectable third-space fluid collections • Ongoing or recent yellow fever vaccination • Unable to interrupt aspirin or other nonsteroidal anti-inflammatory agents for a 5-day period • Unable or unwilling to take folic acid, vitamin B_{12} supplementation, or corticosteroids • Pregnant or breastfeeding

Abbreviations: ANC, absolute neutrophil count; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumors[15]; TS, thymidylate synthase; ULN = upper limit of normal.