



ONS Congress
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Long-term Outcomes of Metformin in Conjunction with Stereotactic Radiotherapy for Early-Stage Non-Small Cell Lung Cancer in a Prospective Phase II Clinical Trial

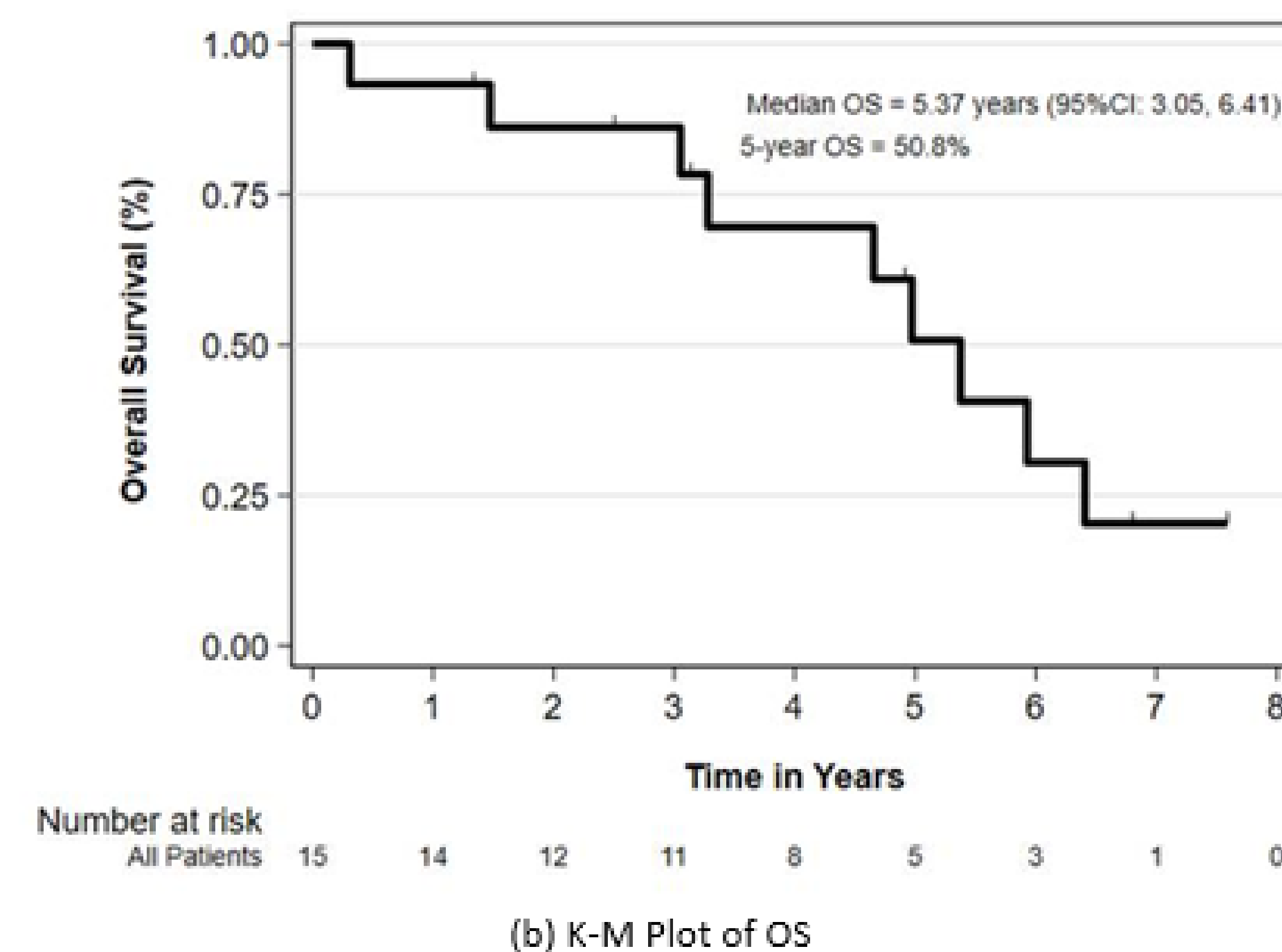
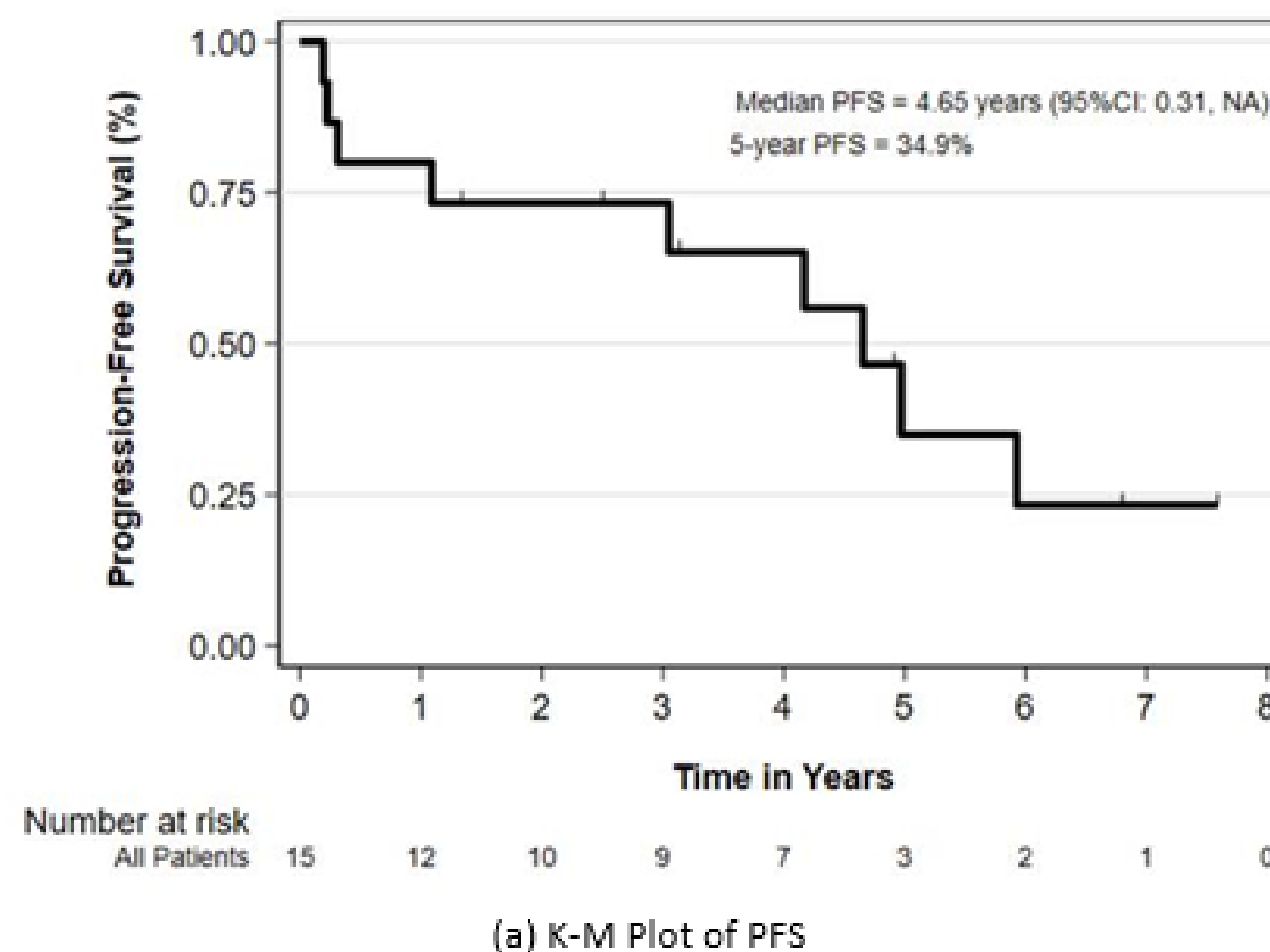
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Significance and Purpose

- Lung cancer remains the leading cause of cancer mortality in the United States.
- Stereotactic body radiotherapy (SBRT) yields high rates of local tumor control for medically inoperable non-small cell lung cancer (NSCLC), however 30-40% of patients develop locoregional or distant progression outside of radiation treatment volumes.
- The dysregulation of 5' adenosine monophosphate-activated protein (AMP) kinases observed in NSCLC warrant analysis of metformin as a potential systemic therapy for NSCLC.

Methods

- Participants with inoperable Stage I-II, cT1-cT2N0M0 NSCLC were randomized to SBRT +/- metformin in a 6:1 fashion and stratified by tumor size (≥ 4 cm vs. < 4 cm) between 2015 to 2017.
- Metformin given at dose of 1000mg daily during week of SBRT and up to 2 weeks post-SBRT.
- Used Response Evaluation Criteria in Solid Tumor (RECIST) to determine time to clinical or radiographic progression, within the primary SBRT field.
- Progression free survival (PFS) was defined as date of randomization to date of local relapse, distant metastasis, or death.
- Overall survival (OS) was defined as date of randomization to date of death with censoring patients alive at last contact.
- Median and 5-year PFS and OS estimates via Kaplan-Meier methodology



Results

- Despite low accrual, 14 patients were randomized to metformin and one to placebo.
- Median PFS was 4.65 years and median survival was 5.37 years. 5-year PFS of 34.9% and OS 50.8%.
- For patients in the metformin group, the 5-year PFS was 27.8% and 5-year OS was 46.0%.
- The patient who received placebo remained alive and without evidence of progression at 5 years.
- Exploratory analyses compared PFS among covariates of interest. Median PFS was slightly lower for patients with other histology relative to patients with adenocarcinoma. Similarly, T1b T-Stage had lower median PFS relative to T1a T-Stage.

Discussion and Implications

- No clear signal of improved outcome of combining metformin with SBRT for inoperable NSCLC.
- Paradoxical results indicating metformin increased tumor marker metabolism.
- The off-target effects of metformin on NSCLC tumor metabolism and signaling remain poorly understood.
- These findings, with the results from NRG-LU001 and OCOG trials, do not support therapeutic use of metformin for NSCLC.
- Of note, the results specific to the covariates of interest and PFS could be useful for future RCT's by inclusion of cancer histology and tumor stage as stratification factors.