Background: Randomized standard doublet chemotherapy (CT) is often clinically equivalent. As newer drugs such as docetaxel (D) and gemcitabine (G) show significant efficacy and favorable toxicity when administered as single agents in the first and second-line setting, sequencing D and G could be an equally effective alternative to CT for palliative therapy. Three studies were conducted to identify optimal single-agent sequences and to compare sequential single agents in a platinum-based doublet.

Methods: Three randomized Phase II trials compared sequential single agents for NSCLC to a platinum-based standard doublet (DCT) in NSCLC patients: GemTax I (n=162), GemTax II (n=160), and GemTax III (n=168). The same inclusion criteria were used in all three studies. Patients with advanced NSCLC, ECOG PS ≤ 2, and greater than or equal to 18 years of age were included. Eligible patients were randomized to receive Arm A (D+G) or Arm B (G+D). Treatment feasibility was measured by the incidence of dose-limiting toxicities (DLTs). Efficacy was measured by ORR, TTP, and survival following treatment assignment.

Results: The use of single agents resulted in higher treatment feasibility and better efficacy profiles compared to the standard platinum-based doublet CT. Treatment feasibility was achieved in 95% of patients in Arm A and 90% of patients in Arm B (p<0.001). Median TTP was significantly longer for Arm A versus Arm B (9.0 versus 5.0 months, Log-rank p=0.004). Median OS was 9.0 versus 5.0 months for Arm A and Arm B, respectively (p=0.03).

Conclusions: The three studies provided evidence supporting the use of single-agent chemotherapy as a less intensive treatment option in patients with advanced NSCLC. The findings suggest that single-agent chemotherapy can be an equally effective alternative to CT for palliative therapy. Sequential single agents could potentially be used as an alternative to CT for patients who are not candidates for CT due to poor performance status or other medical reasons. Further research is needed to confirm these findings and to determine the optimal sequence of single agents for the treatment of advanced NSCLC.