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FOLFIRINOX FOR LOCALLY ADVANCED OR METASTATIC PANCREATIC DUCTAL ADENOCARCINOMA (PDA); CLINICAL OUTCOMES AND PROGNOSTIC FACTORS, THE ROYAL MARSDEN (RM) EXPERIENCE

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Introduction: PDA represents a highly chemo-resistant disease with an extremely poor prognosis. The combination of 5-fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX) has been shown to significantly improve outcomes. However, FOLFIRINOX is also associated with significant toxicity. We conducted this retrospective study to determine the efficacy and toxicity of FOLFIRINOX in patients treated in a single institution outside of a clinical trial.

Methods: We performed a retrospective review of all patients with locally advanced (LA) or metastatic (M) PDA treated with FOLFIRINOX at RM between November 2010 – November 2013. The primary study endpoint was overall response rate (ORR), determined by RECIST 1.1. Secondary endpoints included progression-free survival (PFS), overall survival (OS) and toxicity. Association of survival outcomes with baseline prognostic factors was determined by Cox regression univariate analysis.

Results: 49 pts with PDA were treated with FOLFIRINOX (22 LA and 27 M). Mean age was 60 years and 53.1% were male. Performance status (PS) was 0 in 40.8%, 1 in 49.0% and 2 in 10.2% of pts. FOLFIRINOX was given as first-line treatment in 71.4% of pts and median number of cycles received was 9 (range 1-22). ORR was 42.8% with a further 34.7% of pts having stable disease as their best response. Following FOLFIRINOX, 12 pts (24.5%) underwent surgery (9 LA and 3 M), and an R0 resection was achieved in 66.6%. After a median follow-up of 18.4 months, PFS was 9.5 months (95% CI 7.2 – 11.7) and OS was 13.8 months (95% CI 11.8 – 15.8) for the whole cohort (6.9 months and 10.4 months for pts with metastatic disease). 51% of pts had a reduction in CA19-9 of >50% (including 30.6% with a reduction of >90%). FOLFIRINOX was discontinued in 44.9% of pts due to disease progression. Other reasons for discontinuation included completion of planned cycles (36.7%) and toxicity (4.1%). The most frequently occurring grade 3-4 toxicities were neutropenia (28.6%), fatigue (18.4%), thromboembolism (12.2%), febrile neutropenia (10.2%) and thrombocytopenia (10.2%). Dose delays of ≥7 days occurred in 46.9% of patients; 73.5% of patients required a dose reduction in ≥1 components of FOLFIRINOX and 42.9% of patients had ≥1 hospital admissions. The median duration of hospital admission was 4.5 days. Factors included in the univariate analysis were gender, age (≤ 60 vs. >60 years), T-stage, N-stage, extent of disease (LA vs. M), PS, line of treatment, number of cycles (< 6 vs. ≥ 6 cycles), neutrophil/lymphocyte ratio, baseline CA19-9, CA19-9 nadir (≤ 50 vs. >50), and percentage change in CA19-9 (≤ 50% vs. >50%). Extent of disease (p = 0.044), number of cycles (p < 0.001), CA19-9 nadir (p = 0.001) and percentage change in CA19-9 (p < 0.001) were prognostic for OS.

Conclusion: The efficacy of FOLFIRINOX for PDA at our institution is similar to that reported in clinical trials. Careful selection of patients and monitoring of response (by CA19-9) and toxicities can help maximise advantage in this patient population.