THE ROLE OF CHOI CRITERIA IN ASSESSING RESPONSE TO TYROSINE KINASE INHIBITORS (TKIS) IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC)

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Introduction: Hepatocellular carcinoma (HCC) accounts for 1% of all cancers diagnosed in the United Kingdom (UK) each year with a 5 year survival for patients with advanced disease of less than 5%. Traditional chemotherapeutic agents play a very limited role in the management of HCC. The introduction of Sorafenib, a multitargeted tyrosine kinase inhibitor (TKI) which inhibits tumour proliferation and angiogenesis, has shown a survival benefit of 3 months in patients with advanced HCC and is currently standard of care in the UK. The evaluation of tumour response to chemotherapy has traditionally been assessed using the Response Evaluation Criteria to Solid Tumours (RECIST) tool which examines changes in tumour size. TKIs act by reducing tumour vascularisation and inducing areas of necrosis and cavitation within the tumour. These areas can paradoxically lead to an increase in tumour size despite a response to therapy thus leading to inaccurate reporting of progressive disease if based on RECIST criteria alone. Clinically meaningful responses may therefore be underestimated by the use of RECIST criteria. In 2007, Choi et al suggested a computed tomography (CT) assessment criteria based on tumour density in cancer patients treated with TKIs. Emerging evidence suggests that the Choi criteria correlates more accurately with disease specific survival and provides a more accurate evaluation of tumour response to targeted agents. We aim to evaluate the role of the Choi criteria in assessing response to Sorafenib in patients with advanced HCC.

Methods: From January 2010 to June 2013, 13 patients with a diagnosis of advanced HCC completed a minimum of 3 months treatment with Sorafenib at St Bartholomews Hospital. All patients had a CT scan performed prior to initiation of treatment and after 3 months of Sorafenib therapy. The response to treatment was assessed using both RECIST and Choi criteria by a specialist gastrointestinal radiologist. Agreement between the two classification methods was evaluated with Cohen’s weighted Kappa. Accuracy in restaging was assessed by Kaplan-Meier curve for overall survival with log-rank test according to responders (PR: partial response) versus non-responders (SD: stable disease and PD: progressive disease).

Results: According to RECIST criteria, 15% (2) patients were assessed as having a partial response (PR), 54% (7) with stable disease (SD) and 31% (4) with progressive disease (PD). On assessment with Choi criteria, 38% were considered "responders" (5 = PR) with 62% considered “non-responders” (2 = SD, 6 = PD). Agreement between the two methods was good with a Cohen’s Kappa coefficient of 0.70 (95% Confidence interval 0.46 - 0.94). Due to the small sample size, no significant difference was detected in overall survival according to response type in both methods. (p = 0.27, p = 0.31 for RECIST and Choi respectively). Median overall survival for the patients with PD, SD and PR was 6.5, 16.5 and 16 months respectively according to Choi’s criteria compared to 9.5, 9.0 and 27.5 months according to RECIST criteria.

Conclusion: The use of RECIST criteria may not accurately reflect the response of tumours to TKIs. Alternative radiological assessment using the Choi criteria may provide a more meaningful insight into the anti-tumour activity of targeted agents.