A Phase I Study of Imatinib, Dacarbazine, and Capecitabine in Advanced Endocrine Cancers

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Background: Patients with advanced endocrine cancers, such as adrenocortical carcinoma and medullary thyroid carcinoma, have few well-validated therapeutic options.

Methods: A standard 3+3 dose-escalation design was used with a 21-day cycle, including imatinib on days 1-21, dacarbazine on days 1-3, and capecitabine on days 1-14.

Results: Twenty patients were treated. The most frequent toxicities were edema and fatigue, with dose-limiting fatigue and dyspnea. The recommended phase II regimen is dacarbazine 250mg/m2 daily on day 1-3, capecitabine 500mg/m2 twice daily on days 1-14, and imatinib 400mg daily on days 1-21 of a 21-day cycle. Interestingly, responses were seen in patients with adrenocortical carcinoma, with 1 of 6 patients experiencing a partial response and a second experiencing a minor response, with progression-free survival of 8.8 and 6.4 months, respectively.

Conclusions: The regimen of imatinib, dacarbazine, and capecitabine is well-tolerated. It may have some activity in adrenocortical carcinoma, and further study of this combination or its components may be beneficial for this disease with limited treatment options.