C-34

Secondary Hematological Malignancies Following High-specific Activity Iodine-131 Metaiodobenzylguanidine Treatment of Advanced Pheochromocytoma and Paraganglioma: a Case Series

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BACKGROUND: High-specific activity iodine-131 metaiodobenzylguanidine (HSA I-131 MIBG; AZEDRA®) is the only FDA approved systemic treatment for locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL). Systemic cytotoxic therapies are known risk factors for developing secondary hematological malignancies (myelodysplastic syndrome or acute leukemia). These events were reported in 6 (6.8%) of the 88 patients with PPGL who received a therapeutic dose of HSA I-131 MIBG. To better understand the risk, we undertook a detailed examination of the case reports of patients enrolled in these clinical trials.

METHODS: Two clinical trials (NCT00458952, NCT00874614) were performed to assess the efficacy and safety of HSA I-131 MIBG in patients with advanced PPGL. Adverse events (AEs) were graded according to CTCAE (v3.0) and were coded according to MedDRA (v19.0). Case reports were prepared by compiling and reviewing relevant MedWatch forms for FDA safety reporting (form 3500A) completed by study site investigators.

RESULTS: All six patients who developed a secondary hematological malignancy

(4 MDS, 1 ALL, 1 AML) had been exposed to at least one prior cytotoxic therapy prior to receiving two therapeutic doses of HSA I-131 MIBG (total range: 897.1-1032.54 mCi). These prior treatments included: low specific activity (LSA) I-131 MIBG, chemotherapy and external beam radiation therapy (EBRT) (n=1); chemotherapy and EBRT (n=2), LSA I-131 MIBG and EBRT (n=1); LSA I-131 MIBG only (n=1); and chemotherapy only (n=1). Alternatively, of 23 patients who received HSA I-131 MIBG as first line systemic cytotoxic therapy, none have developed a secondary hematological malignancy as of June 2021.

CONCLUSION: Secondary hematological malignancies following HSA I-131 MIBG treatment for PPGL must be considered in context of the number and intensity of prior cancer treatments. Earlier use of HSA I-131 MIBG in the treatment sequence prior to other cytotoxic agents may reduce the incidence of secondary malignancies.

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