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Comparison of survival outcomes and hypoglycemic control in patients receiving systemic therapy for malignant insulinoma

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BACKGROUND

Malignant insulinoma is a rare neuroendocrine tumor characterized by inappropriate autonomous insulin secretion. The aim of this retrospective review was to evaluate the therapeutic efficacy of various systemic therapies in terms of survival outcomes and clinical management of refractory hypoglycemia.

METHODS

Patients receiving systemic therapy for metastatic or locally advanced, unresectable insulinoma at Mayo Clinic from 1992 to 2024 were retrospectively analyzed. Treatment history, clinical characteristics, and outcomes were collected. Median progression-free survival (mPFS) was calculated from the start date of therapy until documented radiographic progression. Median overall survival (OS) was calculated from the start date of therapy until death or last contact. Determination of hypoglycemic control was based on physician assessment of improvement, stability, or worsening in the severity and frequency of hypoglycemic episodes after initiation of systemic therapy. Survival analysis via Kaplan-Meier method and tests of statistical significance were completed in RStudio.

RESULTS

Fifty-seven patients (male=31) met inclusion criteria. Median age was 52.6 years (range 18-83). Two (3.5%) had MEN1 syndrome. Forty-four (77%) had de-novo metastatic disease. Fifty-two (91.2%) had liver metastases, 11 (19.3%) had distant metastases, and 4 (7%) had regional lymph node metastasis only. Half (50.9%) underwent surgical resection of the primary tumor. Twenty-six (45.6%) underwent liver debulking surgery. Six (10.5%) received ablation or embolization to the primary tumor. Thirty-four (59.6%) received ablation or embolization to liver metastases. Fifteen (26.3%) received radiation therapy. Systemic therapies received included somatostatin analog (71.9%), Everolimus (42.1%), Capecitabine and Temozolomide [CAPTEM] (38.5%), Radioligand Therapy [RLT] (33.3%), Streptozocin-based chemotherapy (14%), other chemotherapy (33.3%), tyrosine kinase inhibitors [TKIs] (7.0%), and immunotherapy (5.2%). mOS and mPFS differed for each systemic therapy (**Table 1**). Durable improvement in hypoglycemic episodes was observed in 93% of patients receiving RLT (**Table 1**). The majority of patients had improvement in hypoglycemia with initiation of CAPTEM (70%) or mTOR inhibitor (61.9%).

Table 1: Survival outcomes and hypoglycemic control for each systemic therapy.

Therapy	Number of Patients	mPFS (months)	mOS (months)	Percent of patients with durable improvement in hypoglycemia
CAPTEM	30	8.13	81.67	70.00
Other chemotherapy	25	5.03	15.23	21.05
Everolimus	24	29.90	74.07	61.90
RLT	22	12.40	49.73	93.33
Somatostatin analog	51	15.00	84.67	35.71
Streptozocin	8	4.32	8.35	33.33

CONCLUSIONS

Overall survival for malignant insulinoma can be several years with appropriate therapy. Systemic treatment with PRRT, CAPTEM, or mTOR inhibitor is very effective for hypoglycemic control.

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