ENDO TOPICAL CATEGORY
TUMOR BIOLOGY

REZOLUTE

A Case Series on the Compassionate Use of Ersodetug, an Insulin Receptor Modulating Antibody, in Patients with Refractory Hypoglycemia Due to Malignant Insulin-Secreting Tumors

SAT-087

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Background

- Tumor hyperinsulinism (HI) is a rare cause of severe, refractory hypoglycemia driven by tumor-mediated excess insulin receptor signaling[1-3]
- It most commonly arises from insulin-secreting pancreatic neuroendocrine tumors or from mesenchymal/epithelial tumors that overproduce incompletely processed IGF-2[1,2]
- Regardless of the upstream driver, both mechanisms converge on excessive insulin receptor activation leading to profound insulin receptor–mediated hypoglycemia[1,2]
- Clinical manifestations include adrenergic, cholinergic, and neuroglycopenic symptoms (for example tremor, diaphoresis, confusion, seizures, and loss of consciousness) with substantial morbidity[3,4]
- Many patients are not cured or are ineligible for tumor-directed therapies, and existing medical options frequently fail to provide durable, stable glycemic control, underscoring a major unmet need[4,5]
- Ersodetug, a fully human monoclonal antibody that selectively and reversibly attenuates insulin receptor signaling at an allosteric site, offers a novel, pancreas-independent approach to treating hypoglycemia across diverse forms of hyperinsulinism[6-8]

Objective

We examined the real-world outcomes from a case-series of patients with refractory hypoglycemia due to metastatic insulin-producing neuroendocrine tumors who received ersodetug for compassionate use as part of an EAP

Methods

- As of the data cut, 9 patients with refractory hypoglycemia due to malignant insulinoma had received ersodetug and are included in this retrospective case series report
- All patients received ersodetug in open-label fashion at doses of 6 or 9 mg/kg every 1-2 weeks initially, followed by a frequency of every 2-4 weeks as tolerated, as add on to standard of care (e.g. diazoxide, somatostatin analogues, etc.), which could be weaned as appropriate
- Glycemic and safety outcomes were reported and analyzed descriptively with a focus on the change from baseline in the GIR as a function of hypoglycemia

Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8*	Patient 9
Gender (M/F) / Age (Years)	M / 55	F / 50	F / 50	F / 43	M / 74	M / 62	M / 74	M / 53	M / 24
Diagnosis	Metastatic Insulinoma	Metastatic Insulinoma	Neuroendocrine Carcinoma of the Cervix	Metastatic Insulinoma	Metastatic Insulinoma	Metastatic Insulinoma	Metastatic Insulinoma	Metastatic Proinsulinoma	Metastatic Insulinoma
No. of Anti-hypoglycemic Therapies at Enrollment	4	3	3	4	4	3	5	2	4
GIR (mg/kg/min) at Ersodetug Initiation	6.0	7.0 (home TPN)	5.1	6.2	4.9	n/a (ambulatory)	5.6	Unknown amount	3.1
Ersodetug Dose Regimen (Dose / Frequency)	6-9 mg/kg every 1-4 weeks	6-9 mg/kg every 1-2 weeks	9 mg/kg every 1-2 weeks	9-12 mg/kg every 1-2 weeks	9 mg/kg every 1-3 weeks	9 mg/kg every 1-2 weeks	6-9 mg/kg every 1-2 weeks	9 mg/kg every 1-2 weeks	9 mg/kg every 1-3 weeks
Percent Reduction in GIR by 8 weeks of Ersodetug Treatment#	>50%, then 100% by 9 weeks	<50%	100%	100%	100%	n/a	100%	Unknown amount	100%
Time to IV Glucose Discontinuation (Days)	74	139(achieved 50% reduction)	4	5	2	n/a	3	n/a	42
Length of Hospitalization Prior to Ersodetug (Days)	28	n/a (ambulatory)	15	49	34	n/a (ambulatory)	4	Unknown duration	16
Baseline ECOG	3	2	3	3	3	1	1	3	1
ECOG at Month 3 on Ersodetug	0	2	0	0	0	0	1	5	0
Total Duration of Ersodetug Therapy (Months)	13	5	5	14	22 (ongoing)	18 (ongoing)	6	1.5	10
Overall Survival (Months)	14	5	5	14	22 (living)	18 (living)	6	1.5	10

* Patient was critically ill when treatment commenced and died of sepsis prior to determination of whether there was a therapeutic effect
# Duration of treatment in Phase 3 upLIFT study

- All patients tolerated ersodetug with no drug-related serious adverse events
- Seven of the 8 patients receiving parenteral glucose at baseline achieved at least a 50% reduction ('responder'; highlighted in table above)

Key Takeaways

- safe and well-tolerated
- associated with marked to complete reduction in parenteral glucose dependence and enhanced functional status
- These findings support the development of an ongoing Phase 3 study of ersodetug in patients with insulinoma and paraneoplastic NICTH (NCT06881992)

Abbreviations: EAP, expanded access program; ECOG, Eastern Cooperative Oncology Group; GIR, glucose infusion rate; IGF-2, insulin-like growth factor 2; tumor HI, tumor hyperinsulinism

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