Combined Lanreotide Autogel and Temozolomide Treatment of Progressive Pancreatic and Intestinal Neuroendocrine Tumors: The Phase II SONNET Study

In advanced neuroendocrine tumors (NET), antiproliferative treatment options beyond somatostatin analogs remain limited. Temozolomide (TMZ) has shown efficacy in NET alone or combined with other drugs.

SONNET (NCT02231762) was an open, multicenter, prospective, phase II study to evaluate lanreotide autogel 120 mg (LAN) plus TMZ in patients with progressive advanced/metastatic grade 1/2 gastroenteropancreatic (GEP) NET or of unknown primary. Patients could be enrolled at first-line or higher therapy line. The primary endpoint was disease control rate ([DCR], rate of stable disease [SD], partial [PR], and complete response [CR]) at 6 months of LAN and TMZ. Patients with nonfunctioning (NF) NET without progression at 6 months were randomized to 6-month LAN maintenance or watch and wait, patients with functioning (F)-NET with clinical benefit (PR, SD) continued on LAN.

Fifty-seven patients were recruited. The majority of patients received the study drug at second or higher treatment line and had an NET G2. DCR at 6 months LAN and TMZ was 73.5%. After 6 months of further LAN maintenance, 54.5% of patients with F-NET and 71.4% with NF-NET had SD or PR vs 41.7% with NF-NET on observation only. LAN and TMZ were effective in all subgroups analyzed. At 12 months of follow-up, median progression-free survival was 11.1 months. Median serum chromogranin A decreased except in NF-NET on observation. O6-methylguanine DNA methyltransferase promoter methylation appeared to better reflect TMZ response than loss of gene expression. During combination therapy, the most frequent treatment-emergent adverse events grade 3/4 reported were nausea (14%), thrombocytopenia (12.3%), and neutropenia (8.8%). Four deaths were reported resulting from severe adverse events not considered related to study medication.

LAN plus TMZ is a treatment option for patients with progressive GEP-NET with more aggressive biological profile showing a manageable safety profile.

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