Acromegaly Management: Focus on Biochemical Control at ENDO 2026

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Acromegaly, a rare endocrine disorder caused by excessive growth hormone (GH) secretion, presents a complex management challenge for clinicians. Untreated or inadequately controlled disease is associated with significant morbidity and increased mortality, primarily from cardiovascular and respiratory complications.1 The immediate takeaway from ENDO 2026 is that while therapeutic options have expanded, a substantial proportion of patients still do not achieve optimal biochemical control, necessitating a re-evaluation of current treatment algorithms and earlier consideration of combination therapies.

KEY TAKEAWAYS

- The Pivot: Despite advancements, a significant proportion of acromegaly patients do not achieve biochemical control with monotherapy.
- The Data: Biochemical remission rates, defined by normalisation of IGF-1 and suppressed GH, remain below 50% in some real-world cohorts.2
- The Action: Clinicians should consider earlier escalation to combination medical therapy or multimodal approaches in patients failing initial monotherapy.

Acromegaly results from a somatotroph adenoma in the pituitary gland, leading to chronic overproduction of GH and consequently, insulin-like growth factor-1 (IGF-1).1 The long-term sequelae include cardiovascular disease, diabetes mellitus, arthropathy, and an increased risk of certain malignancies.3 The primary goals of treatment are tumour mass reduction, normalisation of GH and IGF-1 levels, and alleviation of symptoms, thereby improving quality of life and reducing mortality.4 Surgical resection of the pituitary adenoma is typically the first-line treatment for most patients. However, complete biochemical remission post-surgery is achieved in approximately 40% to 80% of cases, depending on tumour size and invasiveness.5 For patients with persistent disease or those unsuitable for surgery, medical therapy forms the cornerstone of management. The estimated prevalence of acromegaly ranges from 40 to 125 cases per million population, with an annual incidence of 3 to 4 cases per million.3 Early diagnosis is crucial, as delayed treatment can exacerbate the long-term complications and increase mortality.4

Current Therapeutic Landscape and Unmet Needs

Somatostatin receptor ligands (SRLs), such as octreotide and lanreotide, are the most commonly used medical therapies, targeting somatostatin receptors (SSTR2 and SSTR5) on the adenoma to inhibit GH secretion.6 These agents achieve biochemical control (normalisation of IGF-1 and suppressed GH) in approximately 50% to 70% of patients.7 Dopamine agonists (e.g., cabergoline) are less potent but can be effective, particularly in patients with mild IGF-1 elevation or

co-secretion of prolactin, achieving control in about 30% to 40% of selected patients.8 Pegvisomant, a GH receptor antagonist, blocks the action of GH at target tissues, normalising IGF-1 levels in 70% to 90% of patients, but does not reduce tumour size or GH levels.9

Despite these available options, a significant clinical challenge persists: a substantial number of patients do not achieve biochemical control with monotherapy. Data presented at ENDO 2026 highlighted that real-world remission rates, particularly with SRL monotherapy, can be lower than those reported in clinical trials, sometimes falling below 50%.2 This discrepancy underscores the need for more effective treatment strategies and a personalised approach to patient management. The long-term consequences of uncontrolled disease, even with mild elevations in IGF-1, necessitate a proactive approach to therapy escalation. Patients with larger, more invasive tumours often present a greater challenge for achieving biochemical control, even with multimodal therapy.5

Combination medical therapy is increasingly recognised as a strategy for patients who do not achieve control with monotherapy. Combining SRLs with pegvisomant has demonstrated superior efficacy in normalising IGF-1 compared to SRL monotherapy, with IGF-1 normalisation rates reaching 70% to 90%.10 Similarly, the combination of SRLs with cabergoline can be effective in some patients, particularly those with higher SSTR5 expression or co-secreting tumours.11 Radiation therapy, including conventional external beam radiation and stereotactic radiosurgery, is another option for patients with persistent disease after surgery and medical therapy, though its effects are delayed and it carries risks of hypopituitarism and secondary tumour formation.12 The selection of combination therapy often depends on the patient's prior response to monotherapy, tolerability, and specific tumour characteristics, such as SSTR expression patterns, which can be assessed through imaging or pathological analysis of resected tissue.6

Limitations in current management include the need for frequent injections for SRLs and pegvisomant, which can impact patient adherence and quality of life. Furthermore, predicting response to specific therapies remains challenging, as individual tumour characteristics and receptor expression profiles vary. The cost of long-term medical therapy also represents a significant burden on healthcare systems. Future research is focused on developing novel agents, such as new SSTR subtypespecific agonists and oral formulations, as well as refining biomarkers to guide treatment selection. The ongoing challenge is to identify patients who will benefit most from specific therapies or combinations, moving beyond a trial-and-error approach to a more precision-based medicine model for acromegaly. The development of long-acting formulations and oral agents aims to improve patient convenience and compliance, which are critical for maintaining long-term biochemical control and preventing disease progression.7

For a comprehensive understanding of endocrine disorders and their management, including the principles of biochemical control discussed here, consult the Oxford Handbook of Endocrinology and Diabetes.

CLINICAL IMPLICATIONS

The persistent challenge of achieving biochemical control in acromegaly, as underscored by discussions at ENDO 2026, demands a critical re-evaluation of current treatment paradigms. It is clear that relying solely on SRL monotherapy for an extended period in patients with suboptimal response is no longer tenable. Clinicians should adopt a more aggressive stance, considering earlier escalation to combination medical therapy, particularly with pegvisomant, when initial monotherapy fails to normalise IGF-1 levels within a reasonable timeframe. The long-term morbidity and mortality associated with uncontrolled acromegaly far

outweigh the perceived complexities of combination regimens.

From an industry perspective, the market for acromegaly treatments, currently dominated by companies like Ipsen and Novartis with their SRLs, and Pfizer with pegvisomant, will likely see increased demand for combination strategies. This suggests a need for pharmaceutical companies to support clinicians with clearer guidance on optimal combination sequencing and to potentially explore fixed-dose combinations or co-packaging to simplify treatment regimens. The development of novel oral agents or longer-acting injectables could also address adherence issues and improve patient quality of life, potentially expanding market access and patient uptake.

For patients, the implications are significant. Improved biochemical control translates directly into reduced symptom burden, fewer long-term complications, and ultimately, a better quality of life and potentially increased life expectancy. However, the increased complexity of combination therapies, often involving multiple injections, necessitates robust patient education and support programs. It is incumbent upon healthcare providers to ensure patients understand the rationale for intensified treatment and are equipped to manage their regimens effectively, fostering adherence and optimising outcomes. The goal is not just to manage symptoms, but to normalise biochemical markers, and ENDO 2026 reinforces that this often requires a multi-pronged approach.

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