Letrozole improves final height in boys with constitutionally delayed puberty

Aromatase inhibitors are able to block the biosynthesis of estrogen—a process that is essential in bone maturation, growth-plate fusion, and cessation of longitudinal growth. Aromatase inhibitors might, therefore, be used therapeutically to increase adult height.

In a Finnish study by Hero *et al*., 17 boys with constitutional delay of puberty randomly received either testosterone with placebo, or testosterone with the aromatase inhibitor letrozole, for 12 months. Patients were then followed up until they reached near-final height (i.e. their height at a bone age ≥15.75 years). Boys treated with testosterone and placebo reached a mean near-final height of 169.1 cm, compared with 175.8 cm in boys treated with testosterone and letrozole. During treatment, boys in the letrozole group had lower estradiol and higher gonadotrophin concentrations than those in the placebo group. The near-final height of boys in the placebo group was less than their midparental target height; however, this difference was not observed in boys in the letrozole group.

The authors conclude that aromatase inhibitors are a promising tool to improve final adult height in boys with constitutional delay of puberty. Larger studies are needed to confirm the efficacy of aromatase inhibitors in patients with growth disorders, and to investigate the effects of these inhibitors on bone health, maturing spermatogenesis, and carbohydrate and lipid function.

Original article Hero M *et al.* (2006) Treatment with the aromatase inhibitor letrozole during adolescence increases near-final height in boys with constitutional delay of puberty. *Clin Endocrinol* **64:** 510–513

No light shed on national differences in leuprolide dosage regimes

Controlled-release (depot) leuprolide is the preferred treatment for central precocious puberty (CPP). Treatment defers puberty by suppressing gonadotropins: inadequate suppression negatively influences the skeletal maturation and final stature of affected children. For unknown reasons, US clinicians find that adequate gonadotropin suppression requires monthly depot leuprolide doses of 7.50–15.00 mg, whereas their European and Asian counterparts use monthly doses of 3.75 mg. A newer, 3-month depot leuprolide formulation is now available.

Badaru and colleagues, therefore, directly compared the efficacy of three leuprolide dosage regimens in suppressing gonadotropin production, in an open-label, 12-month study carried out in the US. They found that 7.50 mg monthly depot leuprolide provided the best suppression: most patients on low-dose leuprolide (3.75 mg monthly or 11.25 mg 3-monthly) had increased gonadotropin levels, compared with levels while taking 7.5 mg leuprolide. There were no concomitant increases in sex steroid levels, however, and the clinical implications of their findings remain unclear.

All 30 children with CPP were initially given 7.50 mg monthly depot leuprolide for 24 weeks. Patients were assessed at 12-week intervals; the 24 children who achieved luteinizing hormone levels ≤2 IU/l were given 3.75 mg monthly depot leuprolide for a further 24 weeks. The 21 children who maintained adequate luteinizing-hormone suppression (i.e. ≤4 UI/l) were then given a single 11.25 mg dose of leuprolide for the last 24 weeks of the study.

Questions remain as to whether complete gonadotropin suppression is necessary, or desirable, for children with CPP.

Original article Badaru A *et al.* (2006) Sequential comparisons of one-month and three-month depot leuprolide regimens in central precocious puberty. *J Clin Endocrinol Metab* **91:** 1862–1867

Leksell Gamma Knife® radiotherapy in patients with acromegaly

Neurosurgery, pharmacologic, and radiation therapy are all well-established treatment modalities for patients with acromegaly. Ježková and colleagues report on the long-term effectiveness of treatment with the Leksell Gamma Knife® (LGK), alone and in conjunction with other treatment modalities in patients with acromegaly.

The authors investigated 96 patients with acromegaly who underwent treatment with LGK at a large medical center in the Czech Republic. Median follow-up was 54 months. Before treatment with LGK, 71 patients had previously