

**Drotrecogin alfa ineffective in children with sepsis (RESOLVE)**

**Clinical question** Is drotrecogin alfa effective in treating children with sepsis?

**Bottom Line** Drotrecogin alfa (Xigris) is no more effective than placebo in improving outcomes in children with sepsis.

**Synopsis** In this study, 477 children between 38 weeks' gestation and 17 years of age with a suspected or proven infection accompanied by systemic inflammation and sepsis-induced cardiovascular or respiratory dysfunction were randomly assigned (uncertain if allocation was concealed) to receive intravenous infusion of placebo (0.9 per cent saline) or drotrecogin alfa (activated) for 96 hours. The remaining care of the child was left to the discretion of the primary physician. The main outcome, analysed by intention to treat, was a composite time-to-organ-failure score related to cardiovascular, respiratory and renal function. Only three children did not complete the study. At the end of the study, there was no difference in scores between the groups. Additionally, the 28-day mortality rate was the same in each group (17.5 per cent for placebo and 17.2 per

cent for the intervention group). There are some safety concerns raised by this study: although the overall rate of bleeding was similar between the two groups, more children treated with drotrecogin alfa had central nervous system bleeding (five versus one during the infusion period [ $P=0.10$ ]; 11 versus five during the 28-day follow-up [ $P=0.13$ ]).

**Level of evidence** = 1b (individual randomised controlled trial with narrow confidence interval).

**Reference** Nadel S, Goldstein B, Williams MD et al for the REsearching severe Sepsis and Organ dysfunction in children: a gLobal perspective (RESOLVE) study group. Drotrecogin alfa (activated) in children with severe sepsis: a multicentre phase III randomised controlled trial. *Lancet* 2007;369:836–843.

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