Randomised clinical trial: a 1-week, double-blind, placebo-controlled study of pancreatin 25 000 Ph. Eur. minimicrospheres (Creon 25000 MMS) for pancreatic exocrine insufficiency after pancreatic surgery, with a 1-year open-label extension.

Abstract:
Pancreatic exocrine insufficiency (PEI) often occurs following pancreatic surgery. To demonstrate the superior efficacy of pancreatin 25 000 minimicrospheres (Creon 25000 MMS; 9-15 capsules/day) over placebo in treating PEI after pancreatic resection. A 1-week, double-blind, randomised, placebo-controlled, parallel-group, multicentre study with a 1-year, open-label extension (OLE). Subjects ≥18 years old with PEI after pancreatic resection, defined as baseline coefficient of fat absorption (CFA)<80%, were randomised to oral pancreatin or placebo (9-15 capsules/day: 3 with main meals, 2 with snacks). In the OLE, all subjects received pancreatin. The primary efficacy measure was least squares mean CFA change from baseline to end of double-blind treatment (ancova). All 58 subjects randomised (32 pancreatin, 26 placebo) completed double-blind treatment and entered the OLE; 51 completed the OLE. The least squares mean CFA change in the double-blind phase was significantly greater with pancreatin vs. placebo: 21.4% (95% CI: 13.7, 29.2) vs. -4.2% (-12.8, 4.5); difference 25.6% (13.9, 37.3), P< 0.001. The mean ± s.d. CFA increased from 53.6 ± 20.6% at baseline to 78.4 ± 20.7% at OLE end (P< 0.001).
Treatment-emergent adverse events occurred in 37.5% subjects on pancreatin and 26.9% on placebo during double-blind treatment, with flatulence being the most common (pancreatin 12.5%, placebo 7.7%). Only two subjects discontinued due to treatment-emergent adverse events, both during the OLE. This study demonstrates superior efficacy of pancreatin 25 000 over placebo in patients with PEI after pancreatic surgery, measured by change in CFA. Pancreatin was generally well tolerated at the high dose administered (EudraCT registration number: 2005-004854-29).