Supplement Table 29. Summary of studies evaluating immune-modulating enteral nutrition in critically ill adults (KQ11)

Study	Nutrients / focus	Design	Participants	Primary outcome	Summary
Pérez-Cruz et al. 2024 [140]	Enteral formulas: immunomodulatory, ω-3, maltodextrins	Prospective cohort study	Single center; 231 critically ill COVID-19 patients, ventilated and prone	Achievement of protein and calorie targets at day 3	EN was safe and well tolerated; ω-3–enriched formula improved protein/calorie target achievement and some immune markers vs. standard formulas.
Li et al. 2024 [141]	Enteral immunonutrition (ω-3 fatty acids, arginine, glutamine, nucleotides) vs. standard EN	Systematic review and meta-analysis of RCTs	Multicenter; 12 RCTs; 1,124 gastric cancer surgery patients	Immune function markers (CD8+, Ig levels, infections)	Enteral immunonutrition improved immune function (↑CD8+, IgG/IgM, prealbumin, ↓infections) in gastric cancer surgery.
De Luis et al. 2010 [142]	Arginine-enhanced enteral nutrition (two doses) in post-surgical cancer	Randomized, double-blind clinical trial	Post-operative cancer patients receiving EN	Infectious complications, LOS, nutritional and immune markers	Higher-dose arginine-enriched EN improved some immune/nutritional parameters; effect on infections and LOS modest and study small.
Liang et al. 2024 [143]	Enteral glutamine supplementation	Meta-analysis and trial sequential analysis of RCTs	18 RCTs; 2552 critically ill adults	Hospital mortality (primary); secondary: infections, LOS	Enteral glutamine did not clearly reduce mortality; possible modest reduction in hospital LOS but overall evidence judged insufficient for routine use.
Das et al. 2017 [144]	Glutamine immunonutrition	RCT (small, single-center)	ICU adults (mixed)	Infectious complications, mortality, LOS (varied)	Small trial suggesting potential benefit of glutamine on some outcomes, but limited by size and design; contributes low-quality evidence.
Arutla et al. 2019 [145]	Enteral glutamine supplementation	RCT	Single center; 40 severe/ predicted severe acute pancreatitis patients (18 glutamine, 22 control)	Infectious pancreatic and peri-pancreatic necrosis, in-hospital mortality	Glutamine-supplemented EN reduced infectious pancreatic complications and mortality in severe pancreatitis, suggesting benefit in this specific population.
Muthukumar & John 2017 [146]	Enteral/oral glutamine supplementation	RCT (post-surgery and accidental injury)	Surgical and trauma patients	Wound healing, infections, LOS (as reported)	Glutamine supplementation was associated with improved clinical recovery markers in some subgroups, but study quality and size limit generalizability.
Ural et al. 2024 [148]	Arginine, ω-3 fatty acids, nucleotides (immunonutrition)	Single-center RCT	Colorectal cancer surgery patients	Body weight, BMI, arm circumference, biochemical markers	Peri-operative immunonutrition positively influenced post-operative nutritional status and some biochemical markers vs. standard EN.
Kaya et al. 2016 [149]	Pre-operative protein-rich nutrition (not classic IMM formula)	Prospective randomized study	Non-small-cell lung cancer surgery patients	Post-operative complications, LOS	Pre-operative protein-rich oral/enteral nutrition tended to reduce complications and support recovery, but is not a pure immune-modulating formula; supports concept of pre-op nutrition optimization.

ω-3, omega-3 polyunsaturated fatty acids; RCT, randomized controlled trial; EN, enteral nutrition; LOS, length of stay; ICU, intensive care unit; BMI, body mass index; IMM, immunonutrition (immune-modulating nutrition).