2nd Meeting of the Nutrition Support Working Group
16th Congress of Asia-Pacific Blood and Marrow Transplantation Group
Oct 31, 2011 (Sydney)

Current Status of Ongoing Clinical Trials of Nutrition Support in Japan

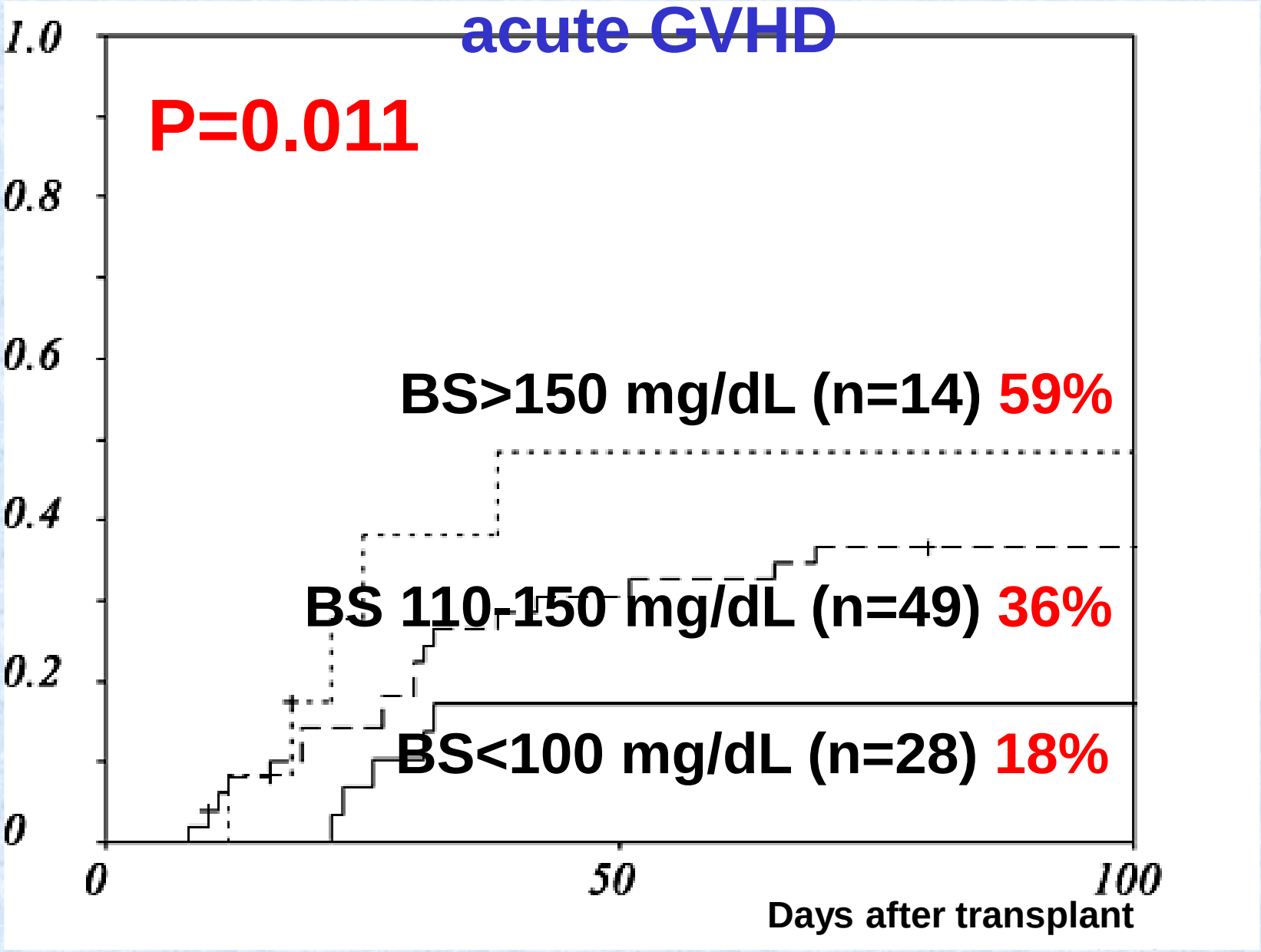
Sung-Won Kim, M.D., Ph.D.

skim@ncc.go.jp

Department of Hematology and Hematopoietic
Stem Cell Transplantation
National Cancer Center Hospital
Tokyo, Japan

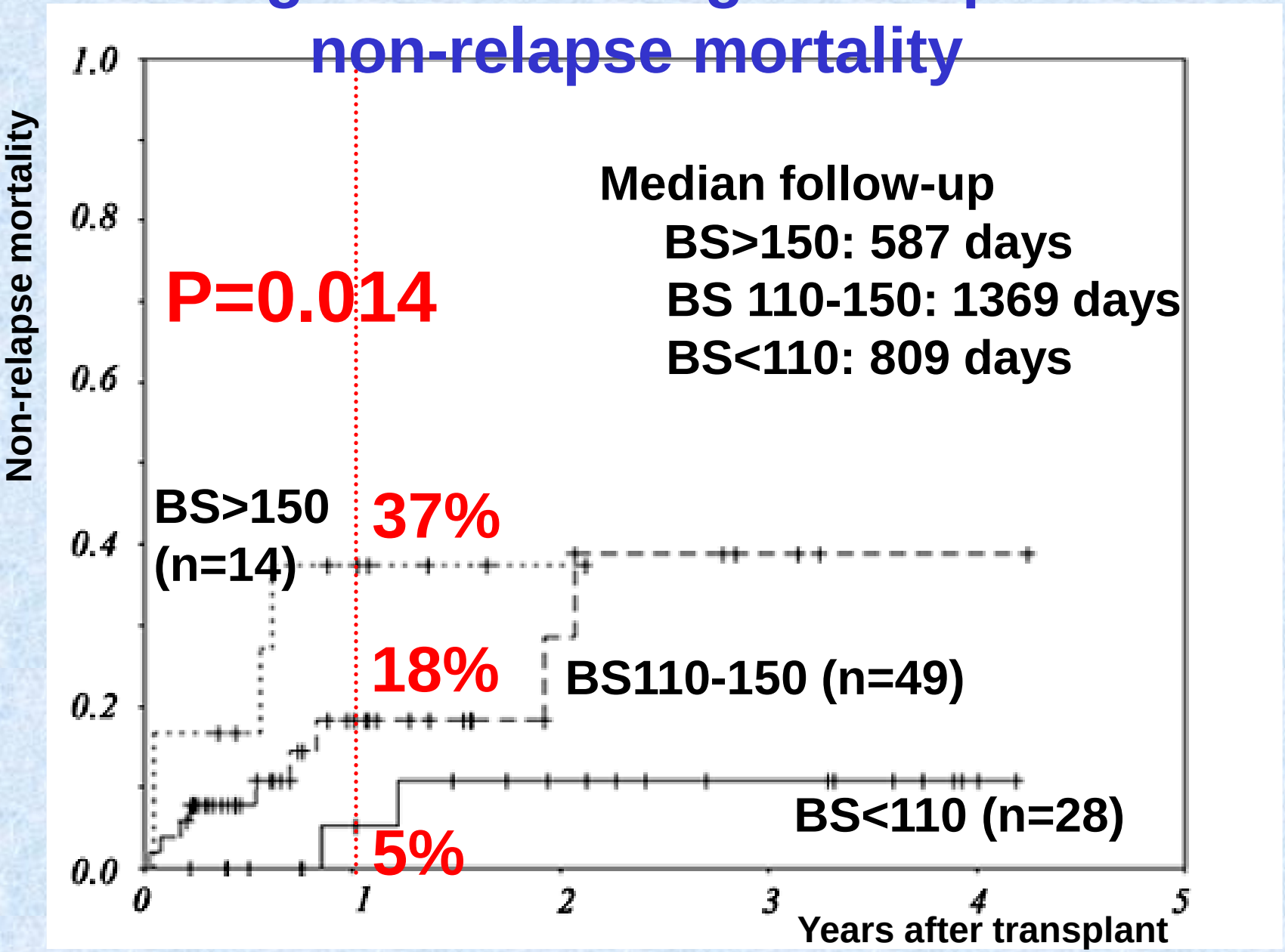
Intensive glucose control and use of fat emulsion

Blood sugar level during neutropenia and acute GVHD



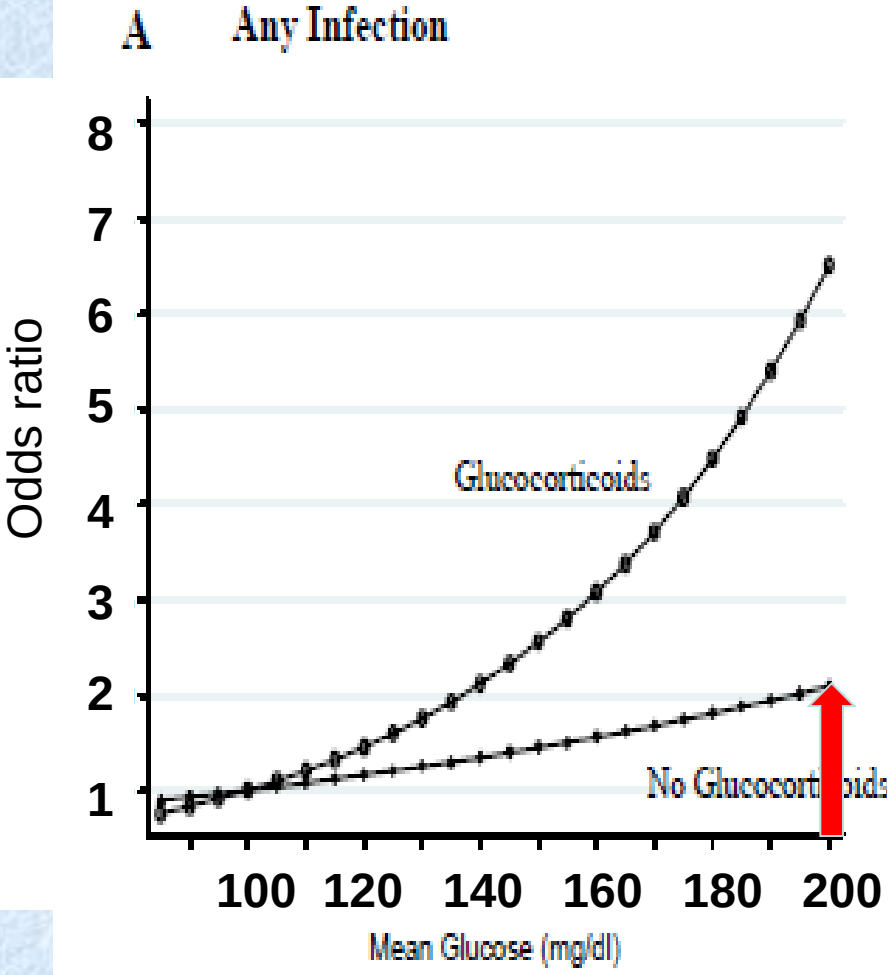
Fuji S, Kim SW, et al. Transplantation 2007; 84: 814-820

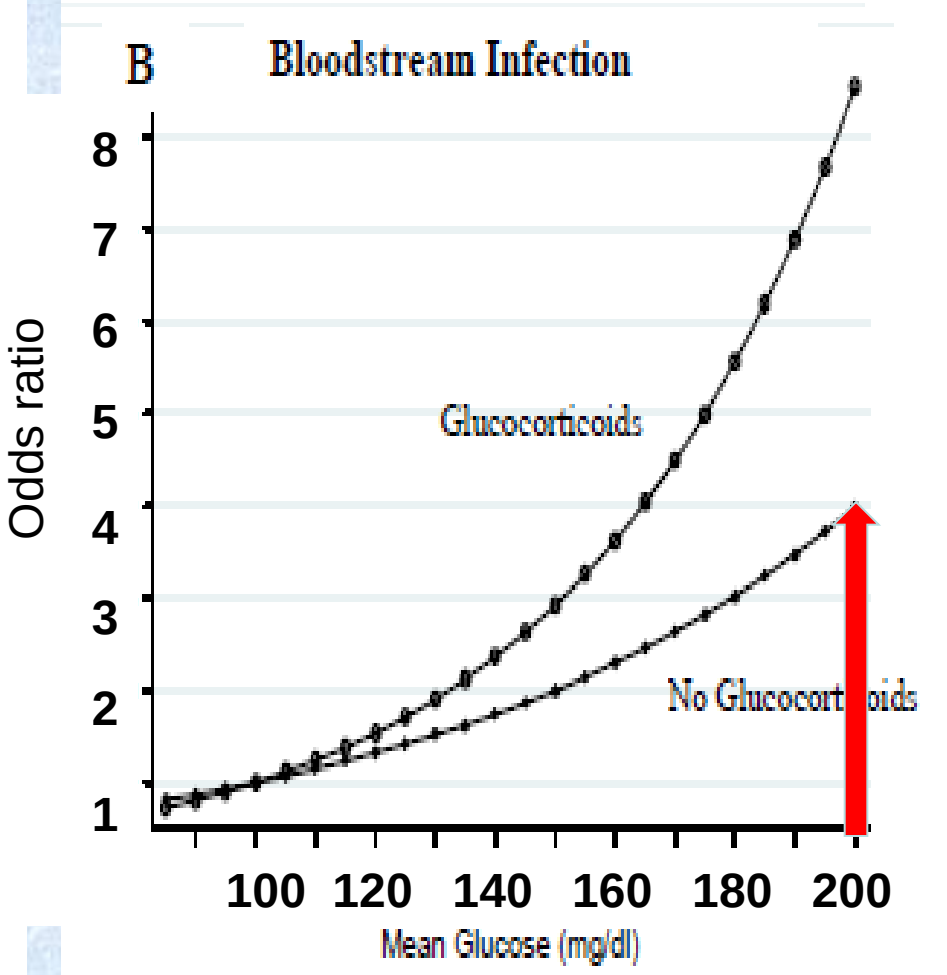
Blood sugar level during neutropenia and non-relapse mortality



Fuji S, Kim SW, et al. Transplantation 2007; 84: 814-820

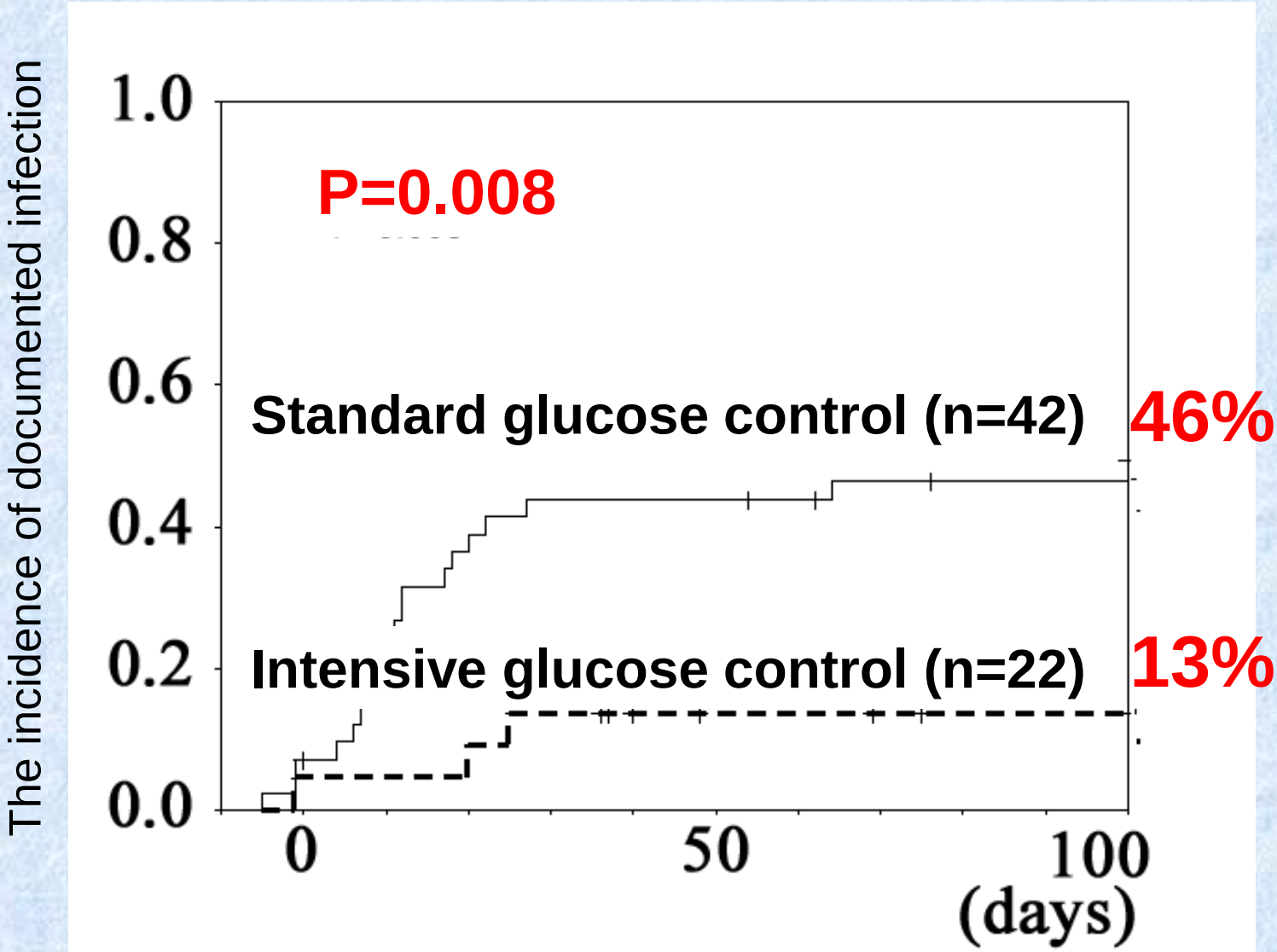
Blood sugar level before HSCT and infection during neutropenia (n=382, Johns Hopkins Institute)





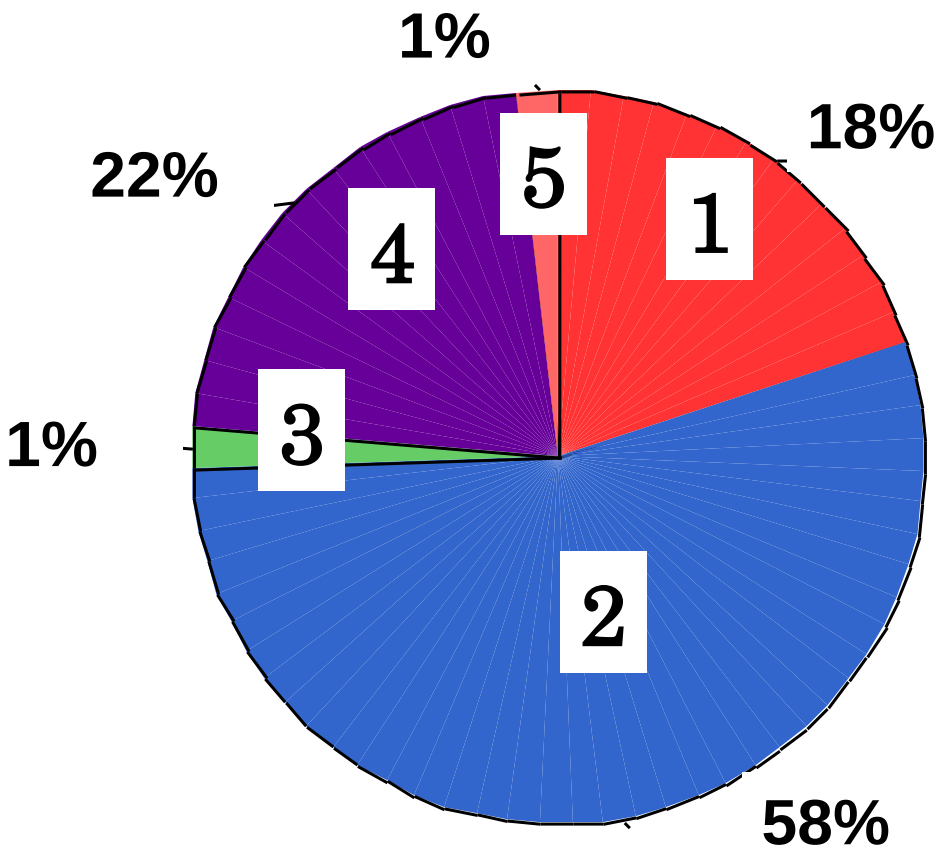
Derr RL, et al. Diabetes Care 2008; 31: 1972-1977

Glucose control during neutropenia and documented infection (matched-control study)



Fuji S, Kim SW, et al. Bone Marrow Transplant 2009; 44: 105-111

Institutional policy of nutrient composition in the parenteral nutrition for HSCT patients - nationwide survey in Japan -



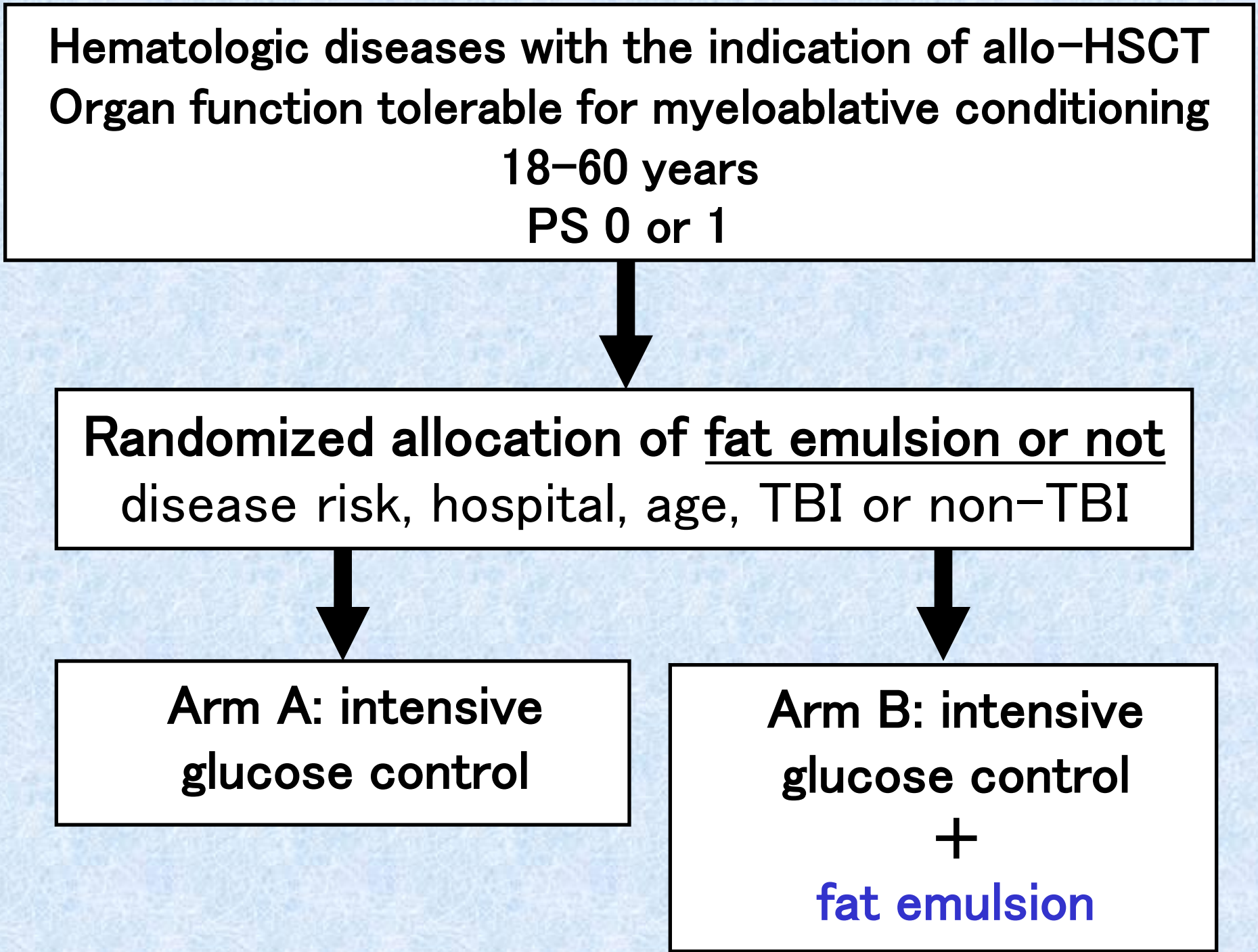
1. carbohydrate + fat + amino acid
2. carbohydrate + amino acid
3. carbohydrate
4. no policy
5. others

Fuji S, Kim SW, et al. JJSPEN 2008; 23: 255-262

Multicenter randomized phase II study of fat emulsion under intensive glucose control for patients who received myeloablative allogeneic HSCT

NST01

- Japanese government research grant study
- To investigate the efficacy of the glucose control with or without administrating fat emulsion (20-30% of total calorie and <0.11 g/kg/h of speed).
- Primary endpoint：the incidence of infection by day 100


Hematologic diseases with the indication of allo-HSCT
Organ function tolerable for myeloablative conditioning
18-60 years
PS 0 or 1
Randomized allocation of fat emulsion or not
disease risk, hospital, age, TBI or non-TBI
Arm A: intensive glucose control
Arm B: intensive glucose control
+
fat emulsion

The Progress of NST01

- **Entry (8/13/2007 - 10/29/2011): 77 pts**
- **Target (- 6/30/2012): 81 pts**
- **Participating Hosp: NCCH (n=69), Osaka City Univ (n=3), Yokohama City Univ (n=3), Tohoku Univ (n=1), Kobe Univ (n=1)**
- **Death: graft & respiratory failure (n=2), relapse (n=2), grade 4 acute GVHD (n=1), VOD (n=1)**
- **No severe adverse event due to administrating fat emulsion and hypoglycemia**

↓

Plan: a phase III study of glucose control in the allogeneic HSCT by the Nutrition Support WG in APBMT

Glutamine and synbiotics

Background

- It is known that glutamine decrease gut toxicity after high-dose therapy. But the efficacy, dose and administration method of glutamine are variable.
- No report of resistant lactobacillus preparation for the patients who received high-dose therapy
- Lactobacillus (probiotics) + glutamine/fiber (prebiotics) = synbiotics

  →expectation of ↑mucosal repair

  and ↑immune function

Multicenter randomized phase II study of synbiotics for lymphoma/myeloma patients who received autologous HSCT

NST02

GFO®（Prebiotics） + Biofermin R®（Probiotics）

- Japanese government research grant study
- To evaluate efficay and safety of synbiotics
- Primary endpoint： grade 3-4 gut toxicity within day 21
- Secondary endpoints：the incidence of infection, total dose of iv opioid, DAO activity, etc

GFO®

Glutamine (3 g/packet)

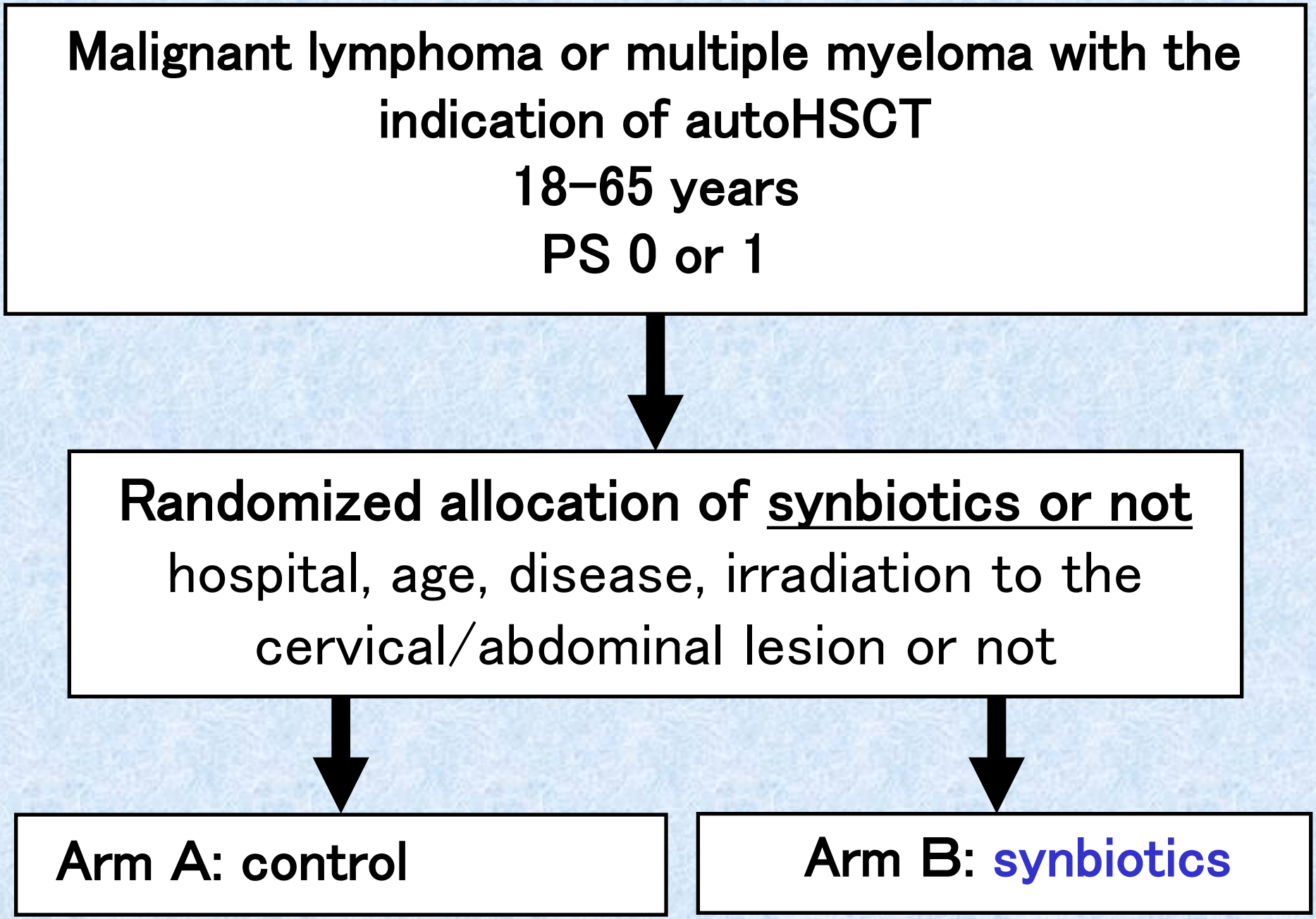
Gln is conditionally essential under aggression. In human blood, gln is the most abundant free amino acid.

Fiber ➡ polydextrose (5 g/packet)

Soluble fiber is broken down into short-chain fatty acid by enterobacteria and utilized.

Oligosaccharide ➡ 4^{G}-β-D-galactosylsucrose (lactosucrose, (1.45 g/packet)

Food for bifidobacteria.


Malignant lymphoma or multiple myeloma with the indication of autoHSCT
18–65 years
PS 0 or 1
Randomized allocation of synbiotics or not
hospital, age, disease, irradiation to the cervical/abdominal lesion or not
Arm A: control
Arm B: synbiotics

The Progress of NST02

- **Entry (11/28/2008 - 10/28/2010): 32 pts**
- **Target (-10/30/2012): 76 pts**
- **Participating Hosp:**

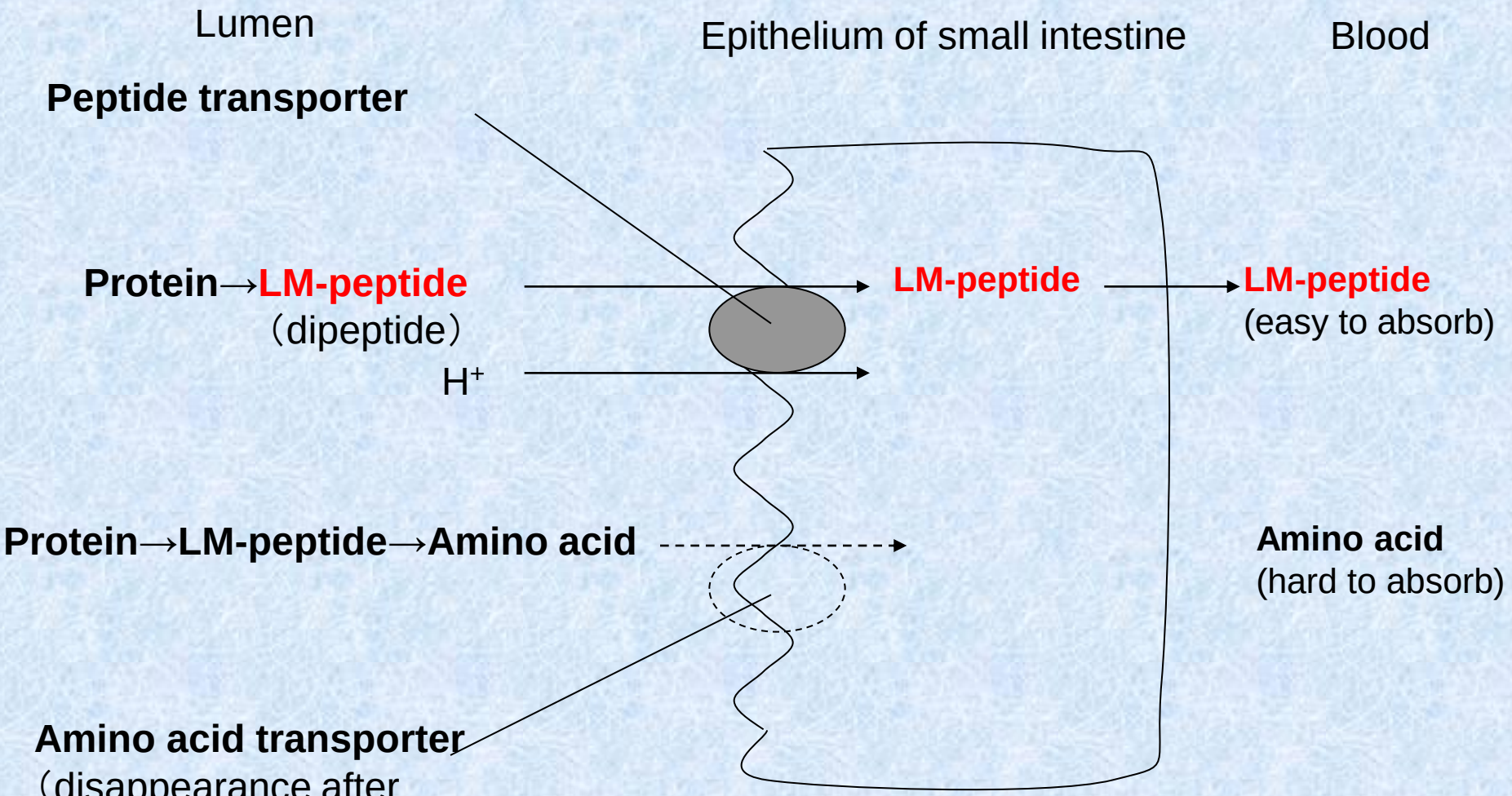
  NCCH

  Ehime Prefecture Central Hosp

  Kumamoto Medical Center
- **No severe adverse event due to administration of synbiotics**

Low-molecular peptide

Digestion and absorption pathway of protein



Guedon C, et al. Gastroenterology. 1986;90:373-378
Tanaka H, et al. Gastroenterology. 1998;114:714-723
Adibi SA. Gastroenterology. 1997;113:332-340
Silk DB, et al. J Parenter Enteral Nutr. 1980;4:548-553

Background

- **Peptide is absorbed more efficient than free amino acid.**
- **There are 18 published RCTs compared LM-peptide and amino acid enteral nutrient. 11 studies had clinical benefit in the LM-peptide arm.**
- **Problems: small cases; various contents into the enteral nutrients**

Multicenter randomized phase II study of low molecular peptide for patients who received reduced-intensity conditioning allogeneic HSCT

NST04

Low-molecular peptide: Peptino®

- Japanese government research grant study
- To evaluate efficacy and safety of low-molecular peptide
- Primary endpoint: grade 3-4 gut toxicity by day 28
- Secondary endpoint: the incidence of infection, total dose of iv opioid, DAO activity, etc

Peptino®

- **Protein 7.2 g (50% dipeptide)**
- **Fat 0 g**
- **Dietary fiber 0 g**
- **Carbohydrate 42.8 g**
- **Osmotic pressure 470 mOsm/L**

Hematologic diseases with the indication of reduced-intensity conditioning alloHSCT
18-70 years
PS 0 or 1

↓

Randomized allocation of LM-peptide or not
hospital, conditioning regimen including Bu, Mel or Cy, stem cell source (BM, PBSC or CB), prior autoHSCT or not

↓ ↓

Arm A: control

Arm B: low-molecular peptide

The Progress of NST04

- **Entry (7/1/2010 - 5/24/2011) : 15 pts**
- **Target (- 6/30/2012) : 76 pts**
- **Participating Hosp:**

  NCCH

  Kumamoto Medical Center

  Tokyo Women's Medical Univ
- **No severe adverse event due to administration of low-molecular peptide**