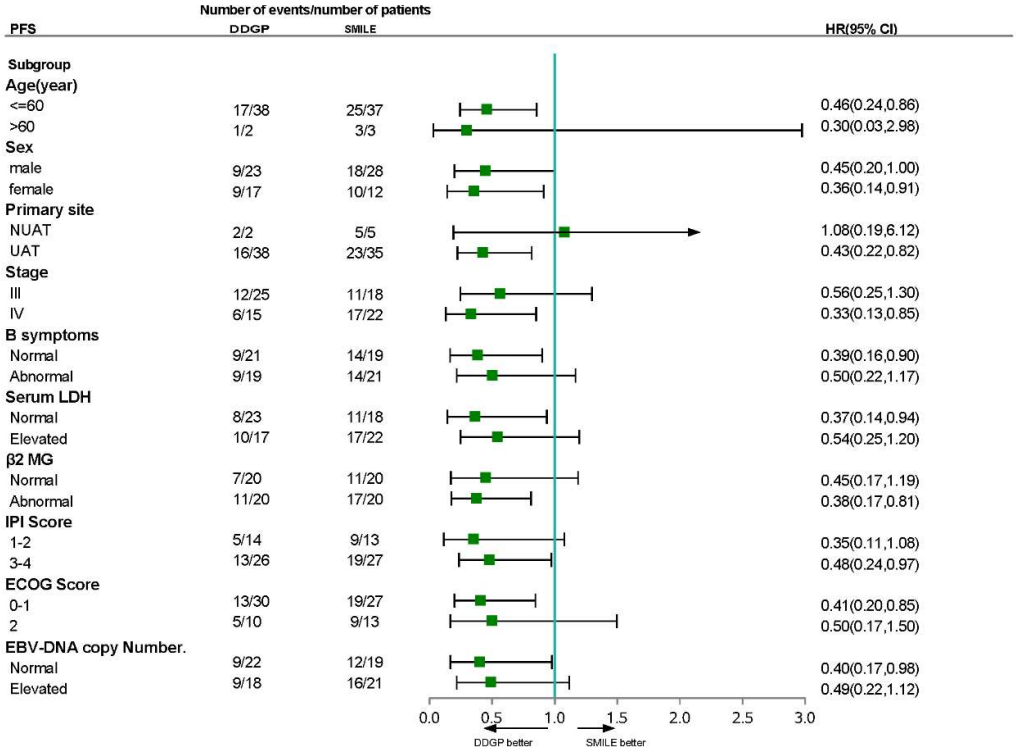
Supplemental Online Content

Wang X, Zhang L, Liu X, et al. Efficacy and safety of a pegasparaginase-based chemotherapy regimen vs an L-asparaginase–based chemotherapy regimen for newly diagnosed advanced extranodal natural killer/T-cell lymphoma: a randomized clinical trial. *JAMA Oncol*. Published online June 16, 2022. doi:10.1001/jamaoncol.2022.1968

This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Subgroup analysis of PFS by key factors

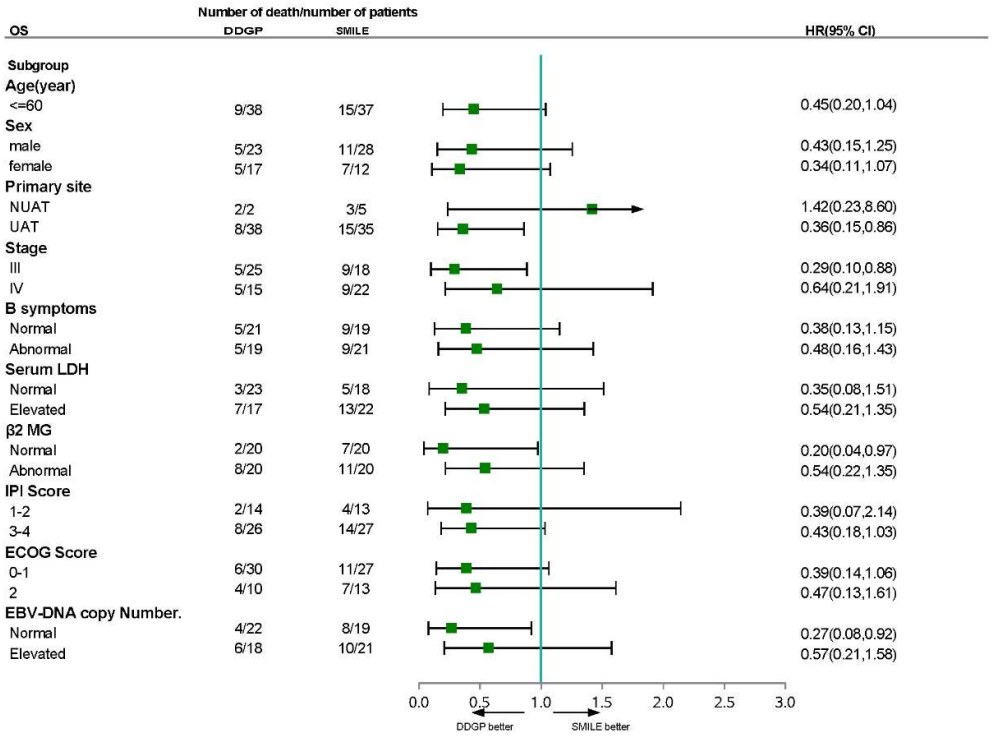
Abbreviations: β2 MG, β2 microglobulin; ECOG, Eastern Cooperative Oncology Group; EBV, Epstein-Barr virus; IPI, international prognostic index; LDH, lactate dehydrogenase; NUAT, non-upper aerodigestive tract; UAT, upper aerodigestive tract.



eFigure 2. Subgroup analysis of OS by key factors.

Since the limited number of patients (five) and events (four) in patients older than sixty, the hazard ratio was infinite and not present in this figure.

Abbreviations: β2 MG, β2 microglobulin; ECOG, Eastern Cooperative Oncology Group; EBV, Epstein-Barr virus; IPI, international prognostic index; LDH, lactate dehydrogenase; NUAT, non-upper aerodigestive tract UAT, upper aerodigestive tract.



eTable 1. Specific treatment regimens

	Dosage		Usage	Time
DDGP regimen				
DDP	20 mg/m^2		ivgtt	d1–4
DEX	15 mg/m^2		ivgtt	d1–5
GEM	800 mg/m^2		ivgtt	d1 and d8
Peg-Asp	2500 IU/m^2 (up to a maximum of 3750 IU)		im	d1
SMILE regimen				
MTX	2 g/m^2		20% iv, 2h; 80% ivgtt, 4 h	d1
DEX	40 mg		ivgtt	d2–4
IFO	1.5 g/m^2		ivgtt	d2–4
L-ASP	6000 U/m^2 (up to a maximum of 10,000 IU)		ivgtt	d3–9
VP-16	100 mg/m^2		ivgtt	d2–4

Abbreviations: DDP, cisplatin; DEX, dexamethasone; GEM, gemcitabine; IFO, ifosfamide; IM, intramuscularly; IV, intravenously; Ivgtt, intravenously guttae; L-Asp, L-asparaginase; MTX, methotrexate; PEG-Asp, pegasparaginase; VP-16, etoposide.

Note: In the SMILE regimen, leucovorin was administered from 12 h after the initiation of methotrexate, 21 mg for the first time, 15 mg for the next time, q6h for a total of 12 times. Blood drug concentration of MTX was measured 24 h (< 10 mmol/L), 48 h (<1 mmol/L), and 72 h (< 0.1 mm mol/L) after the use of MTX.

eTable 2. Treatment-related toxicities and adverse reactions

		DDGP(N=40)			SMILE (N=40)	
		grade			grade	
Adverse Reactions	**0**	**1-2**	**3-4**	**0**	**1-2**	**3-4**
Hematologic						
Leukopenia*	0	15 (37.5)	25 (62.5)	0	6 (15.0)	34 (85.0)
Neutropenia*	0	14 (35.0)	26 (65.0)	0	6 (15.0)	34 (85.0)
Anemia	0	26 (65.0)	14 (35.0)	1 (2.5)	30 (75.0)	9 (22.5)
Thrombocytopenia	3 (7.5)	19 (47.5)	18 (45.0)	3 (7.5)	16 (40.0)	21 (52.5)
Nonhematologic						
Prolonged APTT	27 (67.5)	13 (32.5)	0	24 (60.0)	16 (40.0)	0
Hypofibrinogenemia	26 (65.0)	14 (35.0)	0	27 (67.5)	13 (32.5)	0
Prothrombin time	32 (80.0)	8 (20.0)	0	34 (85.0)	6 (15.0)	0
Hyperbilirubinemia	38 (95.0)	2 (5.0)	0	35 (87.5)	4 (10.0)	0
Transaminase*	25 (62.5)	15 (37.5)	0	16 (40.0)	18 (45.0)	5 (12.5)
Creatinine	39 (97.5)	1 (2.5)	0	40 (100.0)	0	0
BUN	39 (97.5)	1 (2.5)	0	39 (97.5)	1 (2.5)	0

		DDGP (N=40)			SMILE (N=40)	
		grade			grade	
Adverse Reactions	**0**	**1 - 2**	**3-4**	**0**	**1 - 2**	**3-4**
Nausea and vomiting	4 (10.0)	28 (70.0)	8 (20.0)	3 (7.5)	31 (77.5)	6 (15.0)
Mucositis*	40 (100.0)	0	0	27 (67.5)	10 (25.0)	3 (7.5)
Allergy*	39 (97.5)	1 (2.5)	0	31 (77.5)	6 (15.0)	3 (7.5)
Arrhythmia	40 (100.0)	0	0	39 (97.5)	1 (2.5)	0
Pancreatitis	40 (100.0)	0	0	38 (95.0)	2 (5.0)	0

Note: 7 patients in SMILE regimen group reported treatment-related death (6 cases were grade 4 neutropenia induced and 1 case was severe thrombopenia induced). One patient in DDGP regimen group reported treatment-related death (cerebral hemorrhage induced).

* Where the difference of grade 3-4 adverse events between two groups were statistically significant ($P < 0.05$). All the rest were not significantly different ($P > 0.05$).

Abbreviations: APTT, Activated partial thromboplastin time; BUN, blood urea nitrogen.