

# Supplementary Materials

**Table S1.** Patient Clinical and Laboratory Severe Toxicities (grade  $\geq 3$ ) <sup>†</sup>

Adverse events	Pre-DPYD*2A genotyping patients (n = 87)	Post-DPYD*2A genotyping patients (n = 86)	p
Patients with available longitudinal toxicity data	100% (n = 87)	100% (n = 86)	N/A
<i>Mucositis</i>	54% (n = 47)	47% (n = 40)	0.32
Overall severe toxicity	71% (n = 62)	62% (n = 53)	0.18
Clinical toxicity			
<i>Dysphagia</i>	39% (n = 34)	26% (n = 22)	0.058
Pharyngolaryngeal pain	9% (n = 8)	14% (n = 12)	0.32
Pneumonia (including aspiration events)	1% (n = 1)	5% (n = 4)	0.17
<i>Radiation-induced dermatitis</i>	15% (n = 13)	13% (n = 11)	0.68
Xerostomia	1% (n = 1)	2% (n = 2)	0.55
Cellulitis	1% (n = 1)	2% (n = 2)	0.55
Laboratory toxicities			
<i>Neutropenia</i>	8% (n = 7)	9% (n = 8)	0.77
Thrombocytopenia	5% (n = 5)	5% (n = 4)	0.75
Anemia	4% (n = 4)	2% (n = 2)	0.41

In *italic type*: patient clinical and laboratory adverse events most likely related to 5-FU administration. <sup>†</sup> Severe toxicities reported in more than 1% of patients

**Table S2.** Medical Interventions Indicated for Previously Reported Toxicities.

Adverse events	Pre-DPYD*2A genotyping patients (n = 87)	Post-DPYD*2A genotyping patients (n = 86)	p
Patients with available longitudinal toxicity data	100% (n = 87)	100% (n = 86)	N/A
Patients requiring hospitalization			
$\geq 1$ hospitalization	29% (n = 25)	23% (n = 20)	0.41

Median duration (days)	3	6	N/A
	Patients requiring special treatment		
Enteral feeding	41% ( <i>n</i> = 36)	33% ( <i>n</i> = 28)	0.23
Antibiotics	13% ( <i>n</i> = 11)	14% ( <i>n</i> = 12)	0.80
≥ 1 blood product transfusion	3% ( <i>n</i> = 2)	0% ( <i>n</i> = 0)	0.16

**Table S3.** Individual Descriptive Data for Consecutive Patients Identified with DPYD Polymorphisms.

Patient ID	1	2	3	4	5	6	7	8
	DPYD polymorphism							
DPYD*2A mutation	Yes	Yes	No	No	No	No	No	No
Other DPYD variants	No	No	c.2846A> T	c.2846A> T	c.1236G> A	c.1236G> A	c.1236G> A	c.1236G> A
	Patient baseline characteristics							
Age (years)	56	61	73	59	40	52	63	50
Sex	M	M	M	M	M	F	F	M
Smoking status	Past	Never	Past	Past	Past	Past	Past	Never
HSV status	HSV1+	HSV1+	HSV1+	Unknown	HSV1+	Unknown	Unknown	Unknown
p16 antigen status	?	HPV+	HPV+	HPV+	HPV+	HPV+	HPV+	HPV+
Staging (Tx Nx M0)	T4a N1 (IVA)	T2 N2c (IVA)	T1 N3 (IVB)	T3 N2b (IVA)	T2 N2b (IVA)	T2 N2b (IVA)	T2 N2c (IVA)	T1 N2b (IVA)
	Lung ade- noCA (re- sected) HTN							
Comorbidities (descriptive)	HTN	None	Reflux Renal cyst	None	None	Osteop.	None	None
	Treatment characteristics							
Chemoradiotherapy regimen	Cisplatin	Cisplatin	Carbo 5- FU	Carbo 5- FU	Carbo 5- FU	Carbo 5- FU	Carbo 5- FU	Carbo 5- FU
Number of 5-FU cycles completed	N/A	N/A	3	2	2	2	3	3
	Treatment toxicities and medical interventions							
Grade ≥3 toxicities (descriptive)	No	No	Mucositis Thromb.	Mucositis Dyspha- gia PLP Xerost.	Mucositis Dyspha- gia PLP Neutrop.	Mucositis Dyspha- gia PLP	Mucositis Aspira- tion Cellulitis	Mucositis Dyspha- gia

				Aspira-	Feb. neut.			
				tion				
Enteral feeding	No	No	No	Yes	Yes	No	No	Yes
Other treatment (descriptive)	No	No	No	No	Antibiot-	No	Antibiot-	No
					ics		ics	
					G-CSF			
Hospitalization	No	No	No	No	Yes	No	Yes	No
Duration (days)	N/A	N/A	N/A	N/A	5	N/A	4	N/A

### Abbreviations

HTN: hypertension

PLP: pharyngolaryngeal pain

Neutrop: neutropenia

G-CSF: growth colony stimulating factor

Thromb: thrombocytopenia

Xerost: xerostomia

Feb. neut.: febrile neutropenia

Osteop.: osteoporosis