CONGRESO NACIONAL
SOCIEDAD ESPAÑOLA DE FARMACIA HOSPITALARIA
MÁLAGA 15-17 OCT 25

Sapere Aude
Reflexión ante nuevos retos

PERSONALIZACIÓN DE LA TERAPIA FARMACOLÓGICA: FACTORES PARA LA OPTIMIZACIÓN DE RESULTADOS

PERSONALIZACIÓN EN TERAPIA ONCOHEMATOLÓGICA

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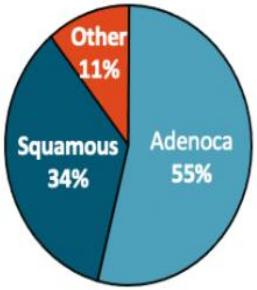
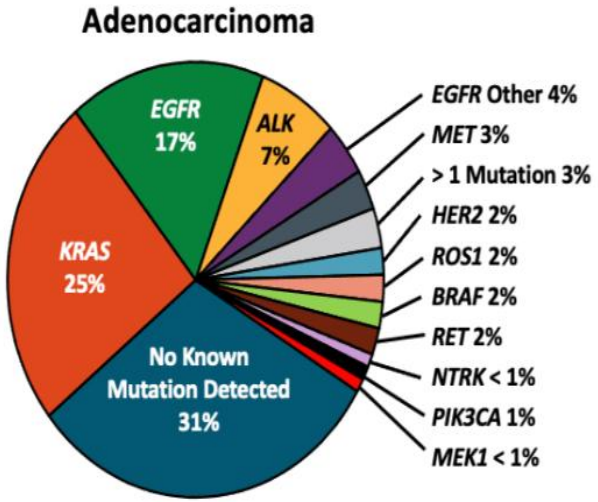
Hospital Duran y Reynals (ICO) / Farmacéutico UPE

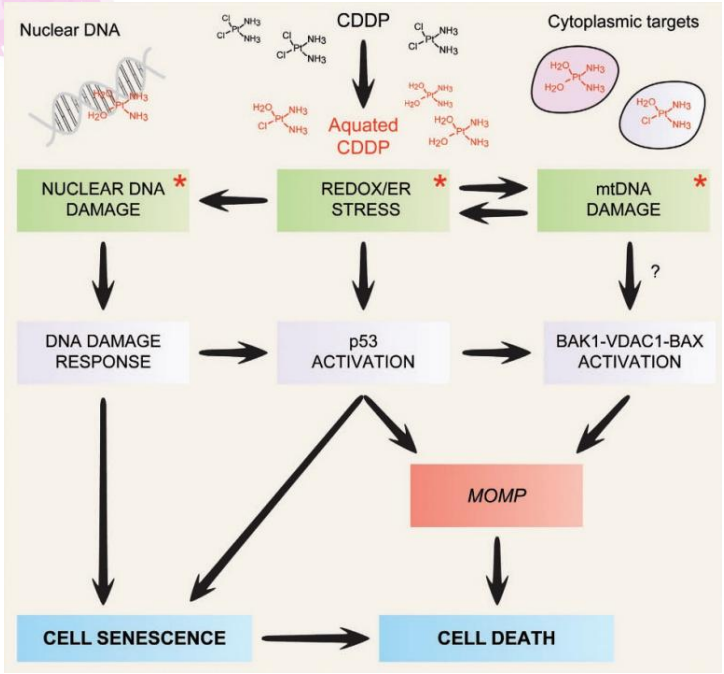
sefh
Sociedad Española de Farmacia Hospitalaria

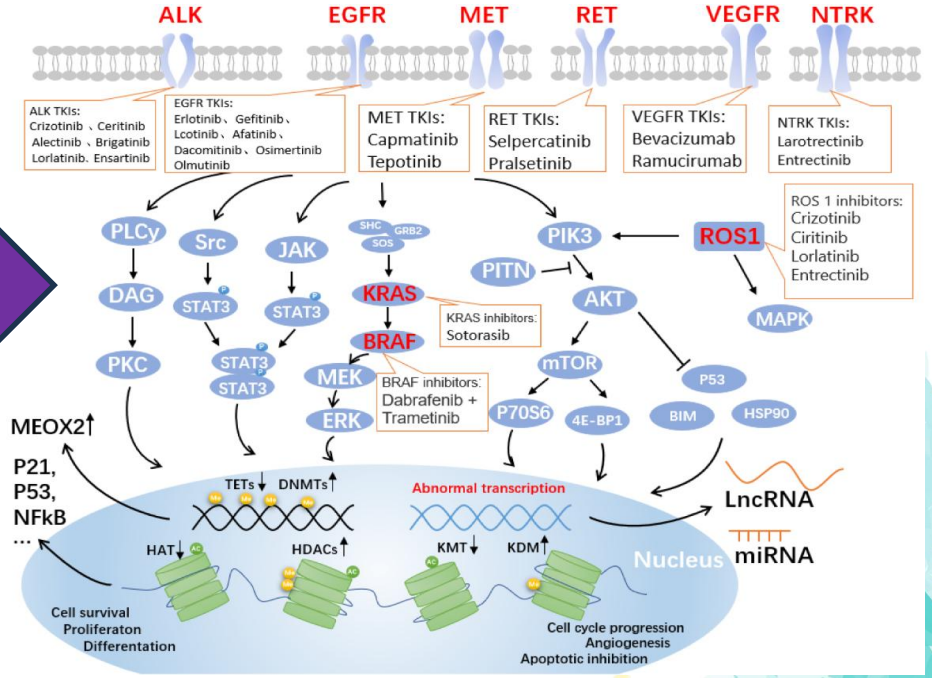
2000 – 2025: MEDICINA DE PRECISIÓN





MEDICINA DE PRECISIÓN





Wu J, Lin Z. Non-Small Cell Lung Cancer Targeted Therapy: Drugs and Mechanisms of Drug Resistance. Int J Mol Sci. 2022 Dec 1; 23 (23):15056.

¿ INDIVIDUALIZACIÓN ?





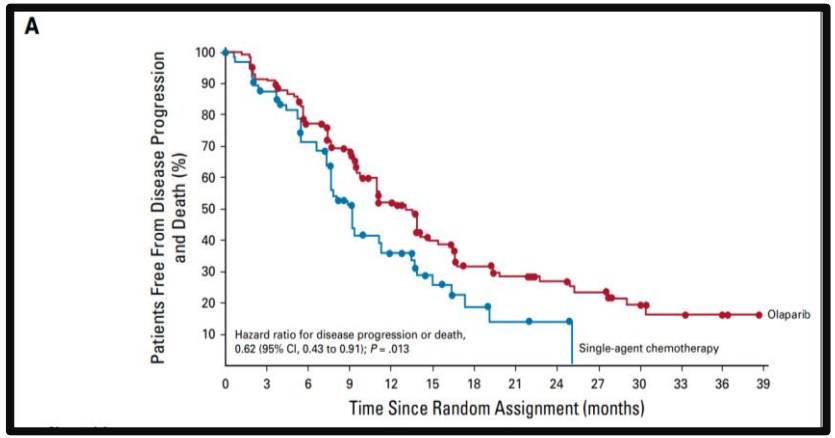

PERSONALIZACIÓN PROACTIVA VS REACTIVA

START

S.C
PESO
DOSI FIJAS
ALTERACIONES CLÍNICAS
VARIANTES GENÉTICAS

EFICACIA/TOXICIDAD

Adverse event	Olaparib (n = 178) Any Grade	Olaparib (n = 178) Grade ≥ 3	Chemotherapy (n = 76) Any Grade	Chemotherapy (n = 76) Grade ≥ 3
Any	174 (97.8)	89 (50.0)	73 (96.1)	36 (47.4)
Leading to dose interruption/delay	85 (47.8)		32 (42.1)	
Leading to dose reduction	48 (27.0)		25 (32.9)	
Leading to treatment discontinuation	13 (7.3)		15 (19.7)	



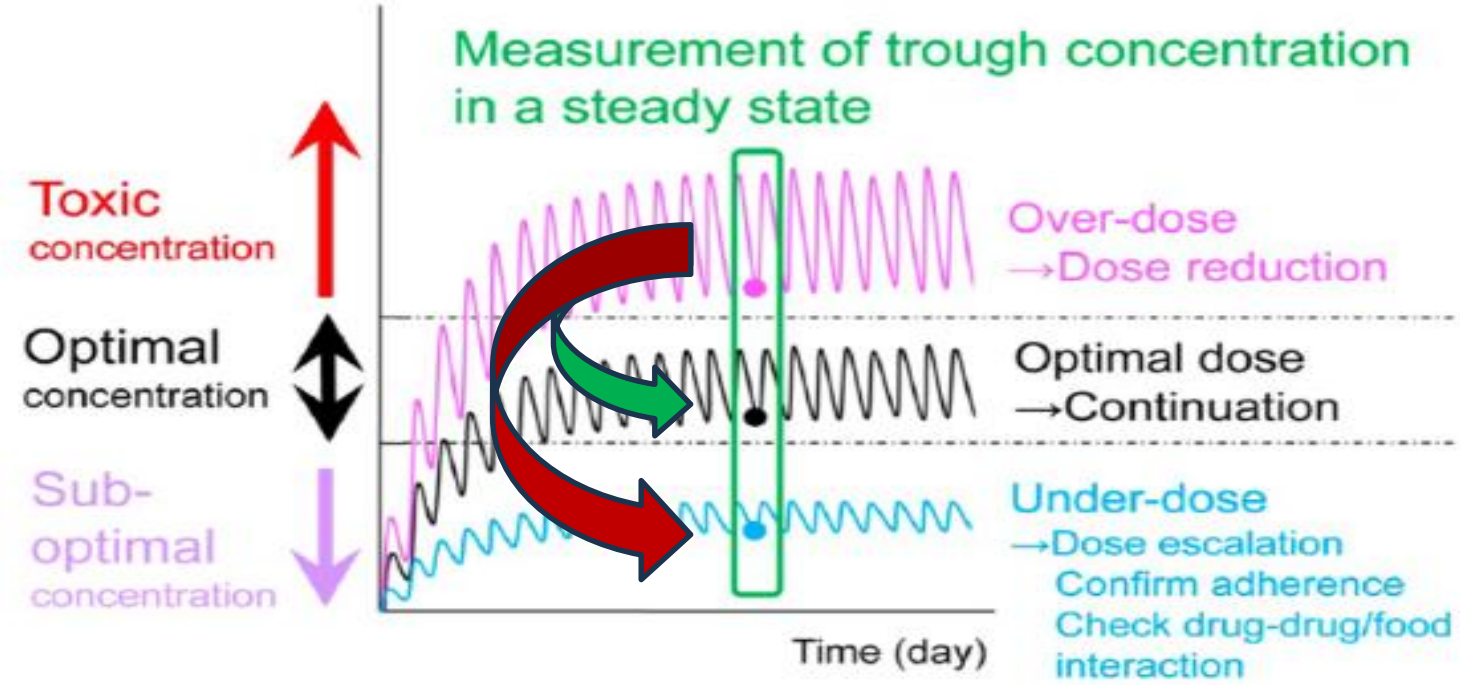
1) QUÉ EXPOSICIÓN SISTÉMICA TIENEN LOS PACIENTES QUE?

A) PROGRESAN?
B) NO PROGRESAN?
C) PRESENTAN TOXICIDAD?
D) REDUCEN DOSIS?
E) ALCANZAN RESPUESTA?

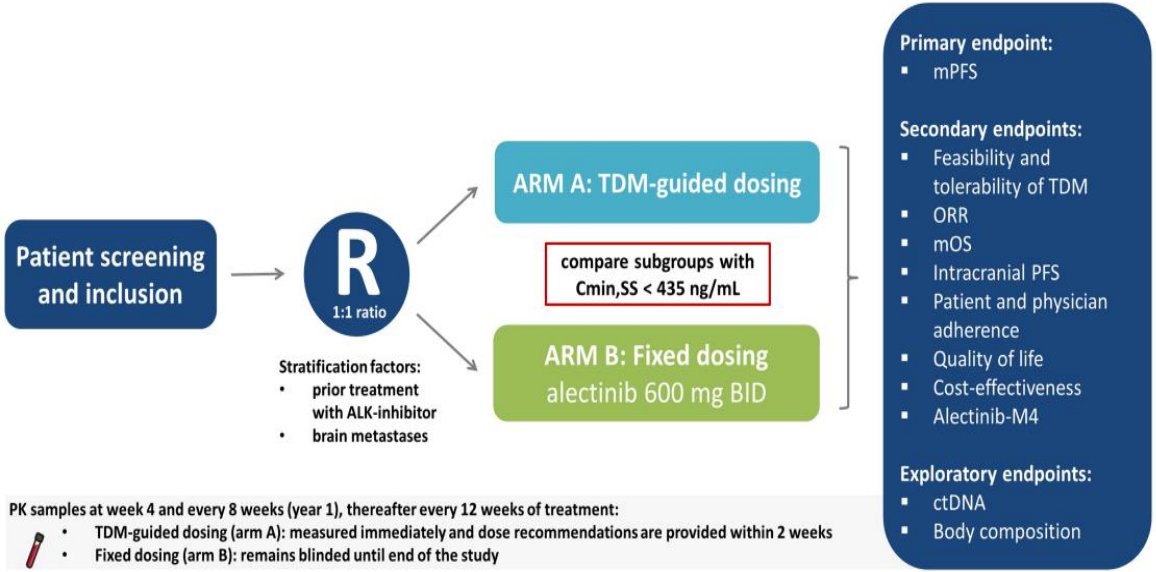
EXISTEN DIFERENCIAS INDIVIDUALES QUE PODRÍAN CONDICIONAR PK/PD, EFICACIA Y TOXICIDAD?

Penson et el. Olaparib Versus Nonplatinum Chemotherapy in Patients With Platinum-Sensitive Relapsed Ovarian Cancer and a Germline BRCA1/2 Mutation (SOLO3): A Randomized Phase III Trial. J Clin Oncol. 2020 Apr 10;38(11):1164-1174

MARGEN TERAPÉUTICO



ADAPT ALECT CLINICAL TRIAL



Dose level	Alectinib Dose
-2	300 mg BID
-1	450 mg BID
0	600 mg BID
+1	750 mg BID
+2	900 mg BID

FIGURE 1
Schematic overview of study design. ALK, Anaplastic lymphoma kinase; BID, twice daily; $C_{min,SS}$, minimum plasma concentration during steady stat
ctDNA, circulating tumor DNA; mPFS, median progression free survival; mOS, median overall survival; ORR, overall response rate; R, Randomizatio
TDM, Therapeutic Drug Monitoring.

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Marinda Meertens et al. Therapeutic drug monitoring guided dosing versus standard dosing of alectinib in advanced ALK positive non-small cell lung cancer patients: Study protocol for an international, multicenter phase IV randomized controlled trial (ADAPT ALEC). Front Oncol. 2023 Mar 9:13:1136221

VARIANTES GENÉTICAS EN ONCOHEMATOLOGIA

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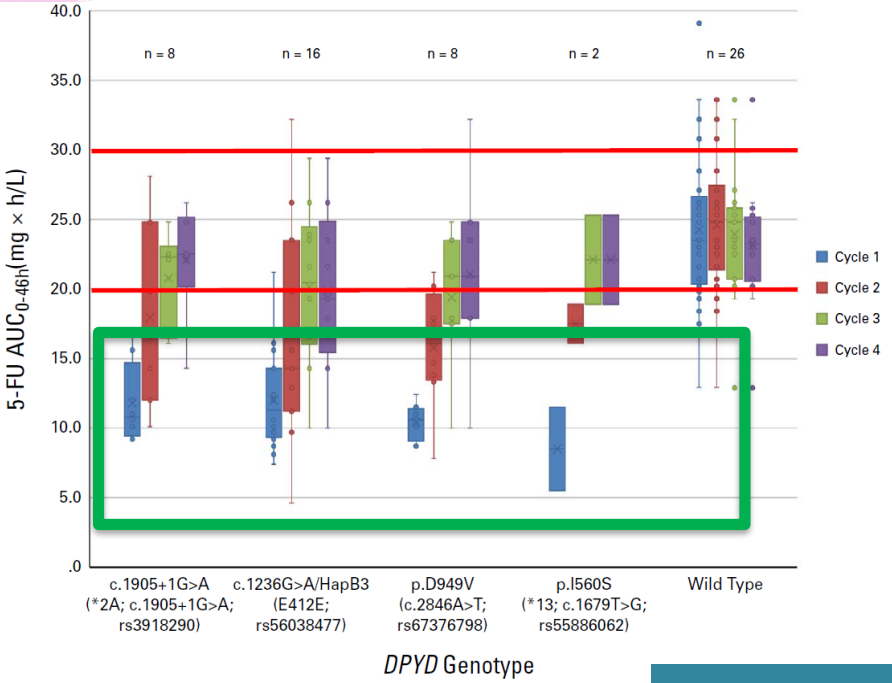
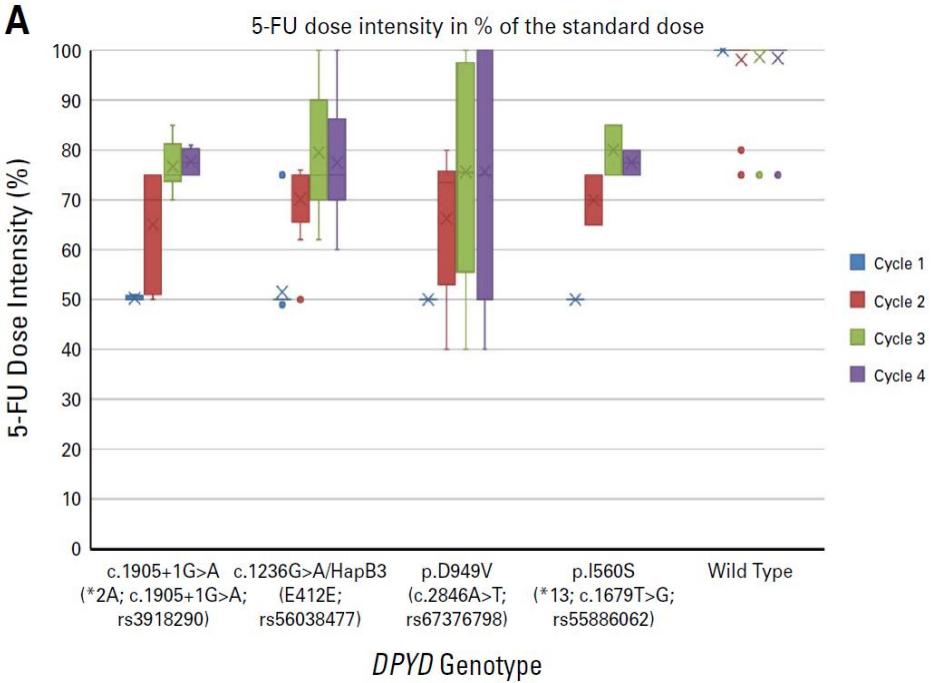
VARIANTES GENÉTICAS DPYD





AUC_1 – AUC_3: 10.1 mg x h/L a 20.2 +/- 4.8 mg x h/L
68% Pacientes AUC > 20 mg x h/L

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Helle-Brit Fiebrich-Westra et al. Precision Treatment of Patients With GI Cancer Using Pre-emptive *DPYD* Genotyping/Phenotyping Plus Pharmacokinetic-Guided Dosing of 5-Fluorouracil. JCO Precis Oncol. 2025 Jun: 9:e2500062. doi: 10.1200/PO-25-00062

PATRONES VARIANTES GENÉTICAS

FARMACOCINÉTICA
rs1045642 del gen *ABCB1*
rs35599367 del gen *CYP3A4*
rs776746 del gen *CYP3A5*

FARMACODINÁMICA
rs10515074 del gen *PIK3R1*,
rs9906827 del gen *RAPTOR*

N Pacientes	ABCB1	PIK3R	RPTOR	CYP3A4	CYP3A5
4	HTZ	WT	HTZ	WT	WT
3	HTZ	WT	WT	WT	WT
2	WT	WT	HTZ	WT	WT
2	HTZ	WT	HMZ	WT	WT
2	HTZ	HTZ	WT	WT	WT
2	HTZ	HTZ	HTZ	WT	WT
2	HMZ	HTZ	WT	WT	WT
2	HMZ	HTZ	HMZ	WT	WT
1	WT	WT	HTZ	WT	HTZ
1	WT	WT	HMZ	WT	WT
1	WT	HZ	HMZ	WT	WT
1	WT	HMZ	WT	WT	WT
1	HTZ	WT	WT	WT	HTZ
1	HTZ	HTZ	HTZ	WT	HTZ
1	HMZ	WT	WT	WT	WT
1	HMZ	WT	WT	WT	HTZ
1	HMZ	WT	HTZ	WT	WT
1	HMZ	HTZ	HTZ	WT	WT

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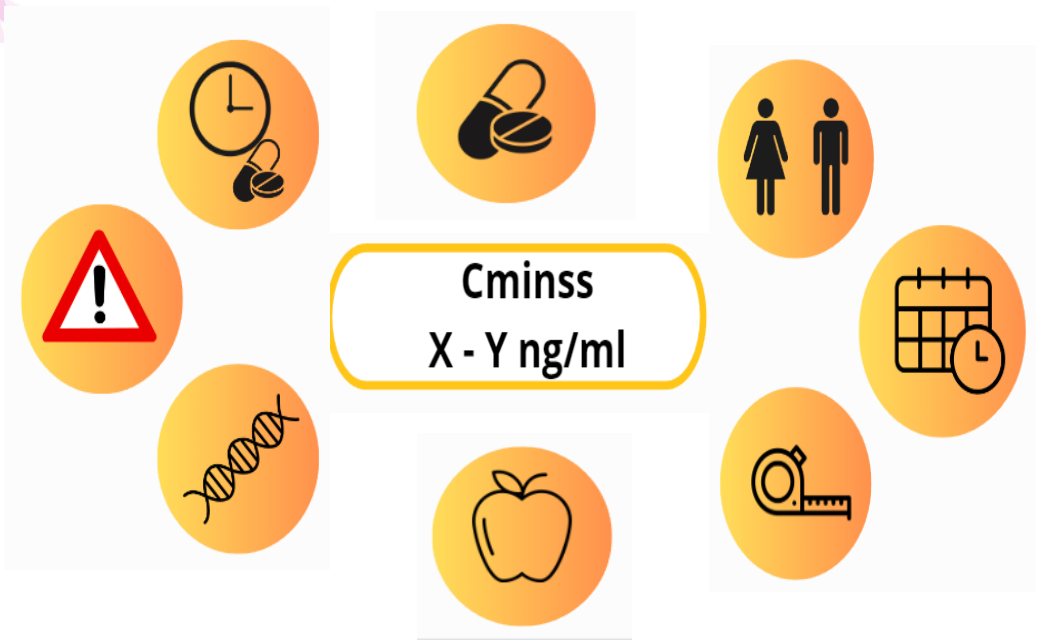
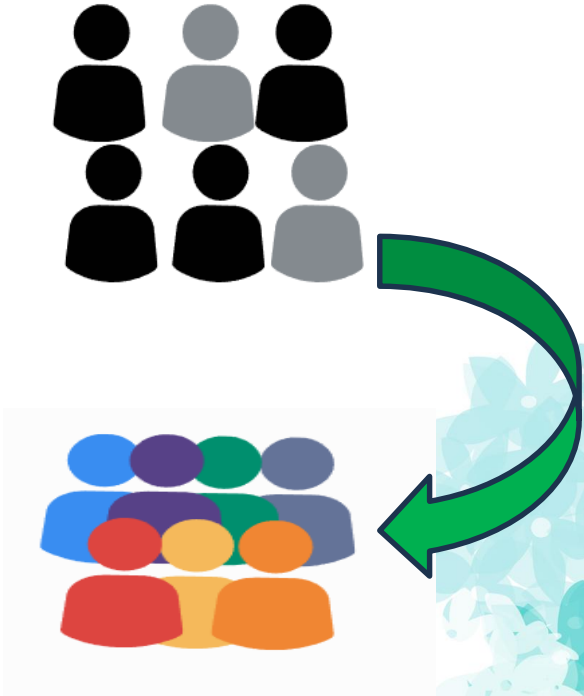
Tomas Pascual et al. Polymorphisms associated with everolimus pharmacokinetics, toxicity and survival in metastatic breast cancer. PLoS One. 2017 Jul 20;12(7):e0180192. doi: 10.1371/journal.pone.0180192.

INDIVIDUALIZACIÓN: ALGO MÁS QUE FARMACOGENÉTICA





PK HOMBRES VS MUJERES

Table 2. Anticancer drugs with documented pharmacokinetic differences between males and females

Drug	Population PK parameter	Reported effect	IIV	*n* (% M)	Ref.
5-Fluorouracil	CL 158 L/h	CL slower in F (−26%) CL faster in M (+26%)	22	26 (NR) 32 (32)	22 23
Atezolizumab	CL 0.235 L/d	CL slower in F (−20%)	29%	1519 (65)	24
Axitinib	CL/F 20.1 L/h	CL/F slower in F (−35%)	39%-94%	237 (NR)	25
Cabozantinib	CL/F 106 L/day	CL/F slower in F (−22%)	35%	289 (70)	26
Carboplatin	CL 107 ml/min	CL slower in F (−31%)	NR	70 (66)	27
Doxorubicin	CL 19.9 L/h/1.8 m^2 for doxorubicinol CL 113.2 L/h in M	CL faster in M ($P = 0.04$) CL slower in F (−50%)	23%	66 (59) 27 (22)	28 29
Epirubicin	CL 95.2 L/h in M	CL slower in F (−23%)	27%	36 (36)	30
Imatinib	CL/F 14.3 L/h $C_{sstrough}$ 1353 ng/ml in M CL/F 11.95 L/h	CL/F slower in F $C_{sstrough}$ lower in M (−25%) CL/F slower in F (−50%)	45%	59 (55) 190 (NR) 43 (63)	31 32 33
Paclitaxel	VM_{EL} 37.4 µmol/h	VM_{EL} maximal elimination capacity higher in M (+20%)	16%	168 (51)	34
Panitumumab	CL 0.273 L/day	CL slower in F (−23%)	NR	1200 (64)	35
Pegylated liposomal doxorubicin	CL 54.6 ml/h/m^2	CL slower in F (−43%)	NR	70 (70)	36
Regorafenib	CL/F 4.02 L/h	CL/F slower in F (−27% for regorafenib and −25% for active metabolites)	NR	62 (61-88)	37
Sunitinib	CL/F 34.1 L/h	CL/F slower in F (−35%) for the active metabolite SU12662	25% for sunitinib and 36% for SU12662	395 (66)	38
Temozolomide	CL/F 10 L/h CL/F 8.8 to 13.9 L/h	CL/F slower in F (−22%)	80.5%	35 (69) 445 (63)	39 40
Topotecan	CL/F 237 L/h in M	CL slower in F (−33%) CL slower in F (−33%)	31%-62%	92 (60) 82 (49)	41,42

$C_{sstrough}$, trough concentration at steady state; CL, clearance; CL/F, apparent clearance; F, females; IIV, inter-individual variability; M, males; NR, not reported; PK, pharmacokinetics; Ref. reference, VM_{EL}, maximal elimination capacity.

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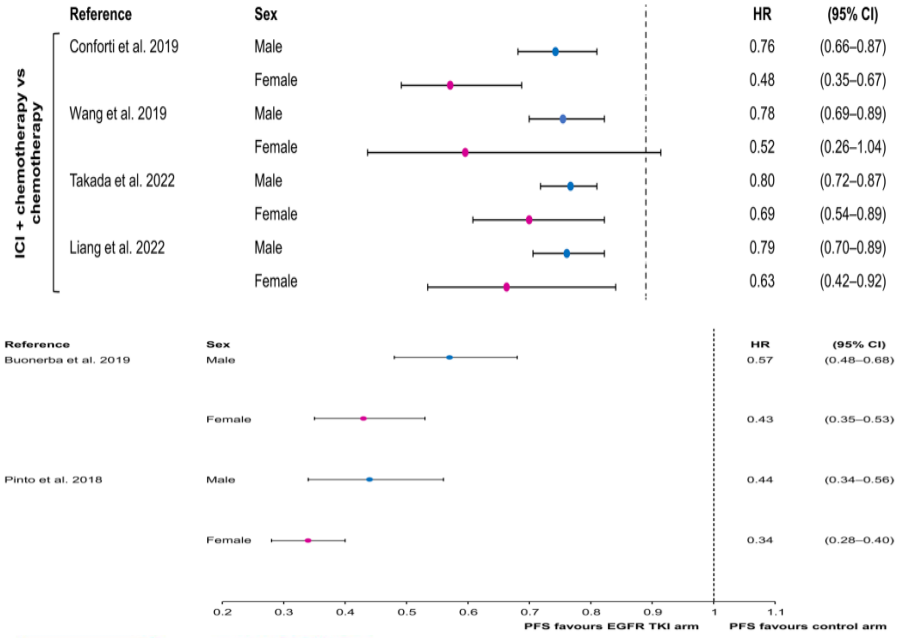
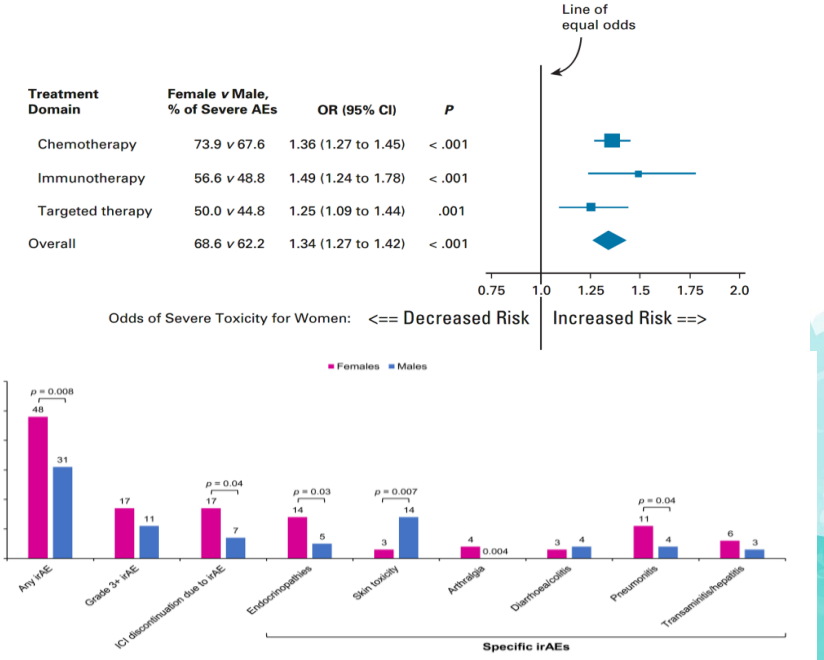
J Delahousse et al. Sex differences in the pharmacokinetics of anticancer drugs: a systematic review. ESMO OPEN. 2024 Dec 19; 9(12):104002

HOMBRES VS MUJERES

EFICACIA



TOXICIDAD



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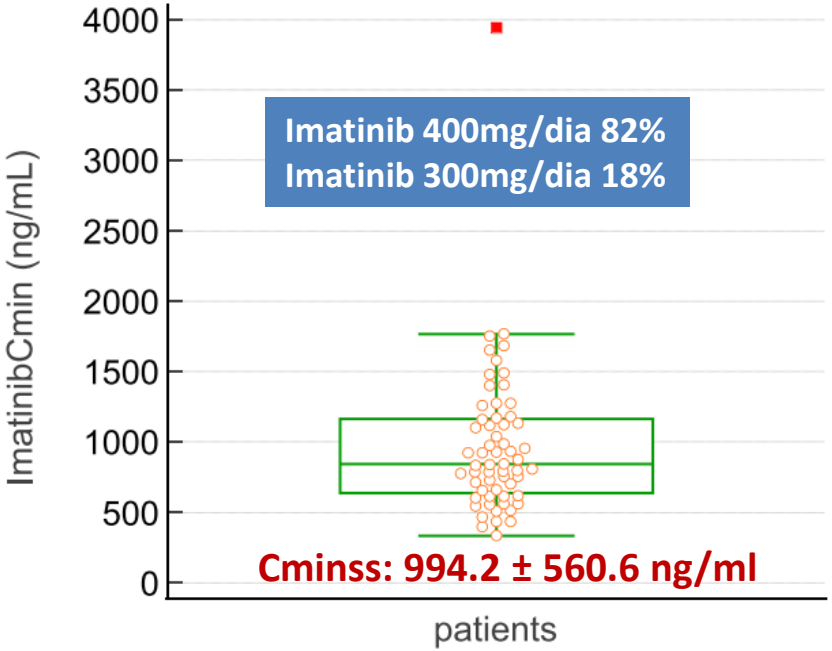
Ana Santaballa Bertrán et al. Sex-related differences in the efficacy and toxicity of cancer treatments. Clin Transl Oncol. 2025 Mar 28. doi: 10.1007/s12094-025-03893-2.

PK - BMI

TABLE 1 Patients characteristics.

Patients characteristics ($n = 60$)	
Age years (mean, range)	56, 18–89
Sex (M/F)	33/27
Body Weight kg (mean ±SD)	72.4 ± 17,8
Height cm (mean ±SD)	167 ± 11,2
BSA m^2 (mean ±SD)	1.82 ± 0,27
BMI (kg/m^2):	
18,5 (%)	10
18,5 < BMI ≤ 24,9 (%)	32
25 ≤ BMI ≤ 29.9 (%)	41
≥30 (%)	17
Co-medications ($n = 35$):	
1 (%)	8.5
1 to 5 (%)	42.8
5 to 8 (%)	37.1
>8 (%)	11.4



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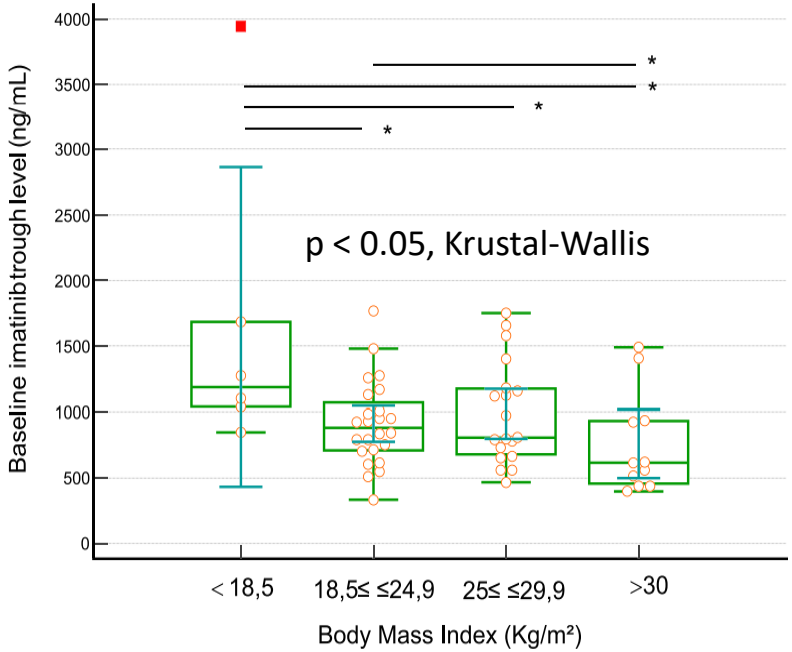
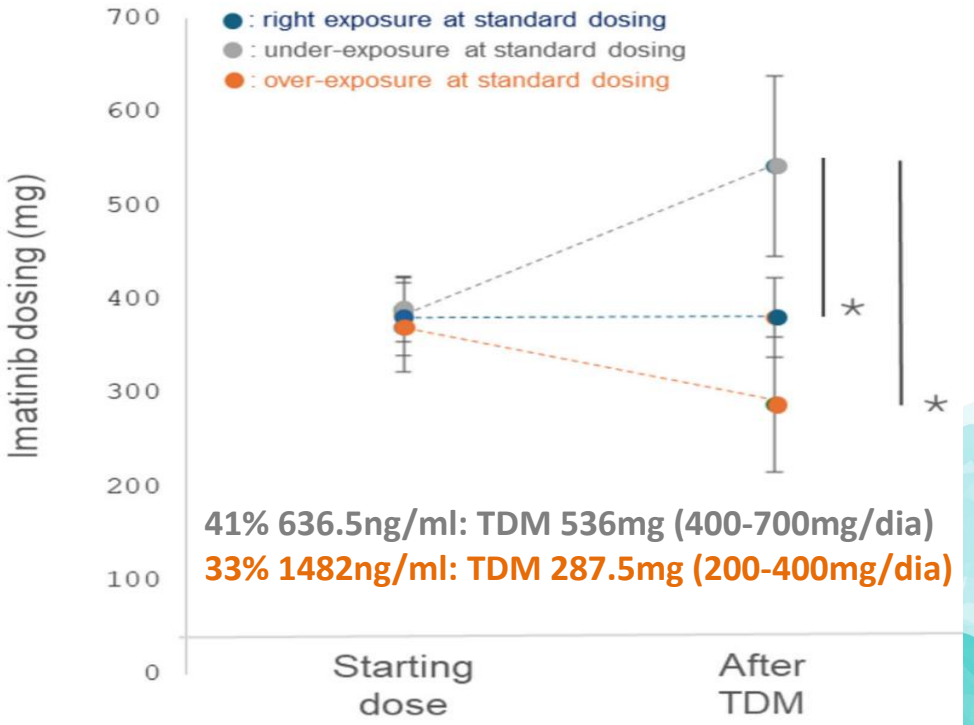
Paul Maroselli et al. Body mass index affects imatinib exposure: Real-world evidence from TDM with adaptive dosing. Fundam Clin Pharmacol. 2025 Feb;39(1):e23049. doi: 10.1111/fcp.13049

PK - BMI





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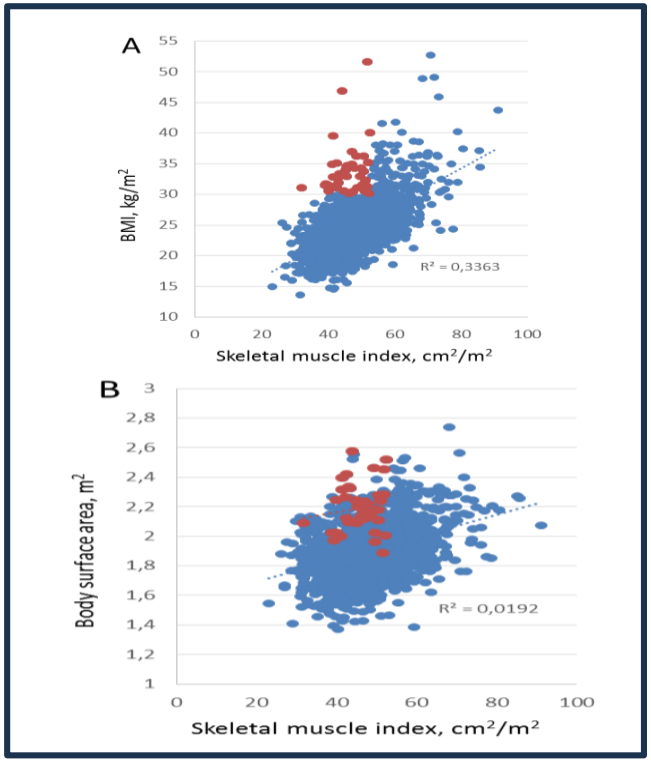
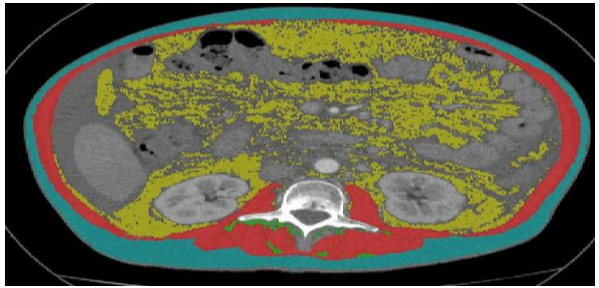
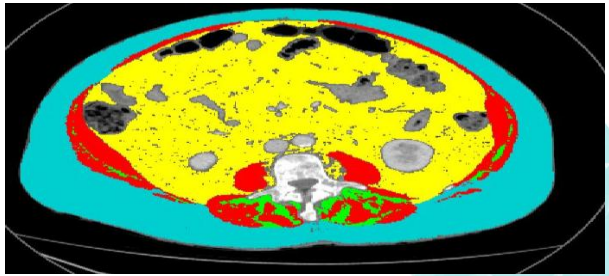
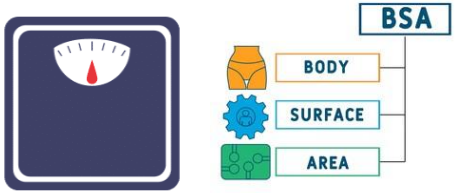
PARÁMETROS ANTROPOMÉTRICOS









INDICE MASA MUSCULAR (SMI)
TEJIDO ADIPOSO SUBCUTANEO (SAT)
TEJIDO ADIPOSO VISCERAL (VAT)
TEJIDO ADIPOSO INTERMUSCULAR (IMAT)

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V E Baracos, L Arribas et al. Sarcopenic obesity: hidden muscle wasting and its impact for survival and complications of cancer therapy. Ann Oncol. 2018 Feb 1;29(suppl_2):ii1-ii9.

COMPOSICIÓN CORPORAL/PK

Study	Cancer type	Type of treatment	N. patients	Age (range)	Body composition evaluation method	Model of PK	Main Results	
							Lean mass	Fat mass
Gusella et al 2002 (11)	Colon	5-fluorouracil	34	Mean 65.5 +/- 9.5 (45-80)	BIA[2]	One or two compartiment model	FFM[4] and TBW[5] better predictors than BW[6] and BSA[7] (multivariate linear regression)	Not measured
Prado et al. 2007 (12)	Stage II/III colon	5-fluorouracil	62	Mean 60.3 +/-9.9	CT[3]	Serum 5FU concentration	Concentration > 20mg 5-FU / kg increased risk of toxicity (OR= 16.75, p=0.013)	Measured but not analysed
Stanisavljevic et al. 2010 (13)	Non-Hodgkin lymphoma	R-CHOP[1]	30	Median 56 (20-82)	BIA[2]	Serum cyclophosphamide concentration	Risk of toxicity for a cyclophosphamide concentration ≥ 27.3 mg/kg (p=0.02)	Risk of toxicity for a cyclophosphamide concentration ≥ 77.9 mg/kg (p=0.0011) Risk of toxicity for a doxorubicin concentration ≥ 4.9 mg/kg (p=0.008)
Prado et al. 2011 (14)	Breast Stage II-III	Epirubicin	24	Median 52.5 (28.1-67.1)	CT[3]	One compartiment model	LBM[8] explains 18 % of variance in epuribicin clearance	Measured but not associated with clearance of epuribicin
Mir et al. 2012 (15)	Hepatocellular carcinoma	Sorafenib	17	Median 62.5 (32-79)	CT[3]	One compartiment model	Median AUC[9] is higher in sarcopenic patients (102.4 mg/l.h) compared in non-sarcopenic patients (53.7 mg/l.h), (p = 0.013)	Not measured
Massicotte et al 2013 (16)	Medullary thyroid carcinoma	Vandetanib	33 (23 treated and 10 placebo)	Mean 51 (27-69)	CT[3]	SerumVandetanib concentration	Higher concentration levels (1091 vs 739 ng/ml, p = 0.03) and lower skeletal muscle mass index (< 43.1 cm2/m2) increased risk of DLT[10].	Not measured
Wong et al 2014 (17)	Breast cancer stage II-III	Doxorubicin Pre-operative or post-operative chemotherapy	44	Mean 50.4 +/- 10.1	CT[3]	Two compartiment model (doxorubicin) sequential compartiment (metabolite) Serum Doxorubicin Concentration and AUC9	BSA[6] and muscle volume did not predicts pharmacokinetics or toxicities.	Positive correlation between doxorubicin AUC[9] and abdominal fat volume and total abdominal fat volume ($r^2 = 0.324$ and $r^2 = 0.262$ respectively, p <0.001)

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S Gérard et al. Body Composition and Anti-Neoplastic Treatment in Adult and Older Subjects - A Systematic Review. J Nutr Health Aging 2016;20(8):878-888.

COMPOSICIÓN CORPORAL/TOXICIDAD

Type of treatment	N. patients	Age (range)	Measure of toxicity	Body composition evaluation method	Thresholds of sarcopenia	Main results	
						Lean Mass	Fat Mass
CHEMOTHERAPY							
5-fluorouracil	62	Mean 60.3 +/-9.9	Grade 3-4 toxicity (NCIC-TC3)	CT[2]	none	Concentration > 20mg 5-FU / kg increased risk of toxicity (OR= 16.75, p=0.013)	Not analysed
Capecitabine	55	Mean 54.8 +/- 10.4 (37-80)	Grade 2 or + toxicity (NCIC-TC3)	CT[2]	<38.5 cm²/m² (women)	Sarcopenia increased risk of toxicity HR = 4.1 (p=0.04)	Not measured
R-CHOP1	30	Median 56 (20-82)	Grade 3-4 toxicity (NCIC-TC[3]) or dose reduction	BIA[3]	none	Risk of toxicity for a cyclo-phosphamide concentration ≥ 27.3 mg/kg (p=0.02)	Risk of toxicity for a cyclophos-phamide concentration ≥ 77.9 mg/kg (p=0.0011) Risk of toxicity for a doxorubicin concentration ≥ 4.9 mg/kg (p=0.008)
FEC2	24	Median 52.5 (28.1-67.1)	Grade 3 or + toxicity (NCIC-TC[3])	CT[2]	none	Sarcopenia associated with toxicity (p =0.002)	Not analysed
5FU + oxaliplatin or irinotecan	51	Median 65 (22-84)	Grade 3-4toxicity (NCICTC[3])	CT[2]	≤ 55.4 cm²/m² (men) ≤ 38.9 cm²/m² (women)	Sarcopenia increased risk of toxicity OR = 13.5 (CI 95 % : 1.08-169.3)	Not associated
Phase I all chemotherapies	93 (50 males ;43 females)	Median 57 (21-77)	grade 3-4 toxicity DIR5 drug interrupting toxicity	CT[2]	Median of population < 54.1 cm²/m² (men) < 40.8 cm²/m² (women)	Sarcopenia associated with DLT and severe toxicity	No association of Visceral adipose tissue or subcutaneous adipose tissus wi'h severe toxicities or drug interrupting toxicities.
Doxorubicin Pre-operative or post-operative chemotherapy	84	Mean 50.4 +/- 10.1	Grade 4 Hematologic toxicity	CT[2]	none	Muscle volume not associated with grade 4 hematological toxicities	High intra-abdominal fat volume predicts for greater Doxorubicin exposure and hematologic toxicities (grade

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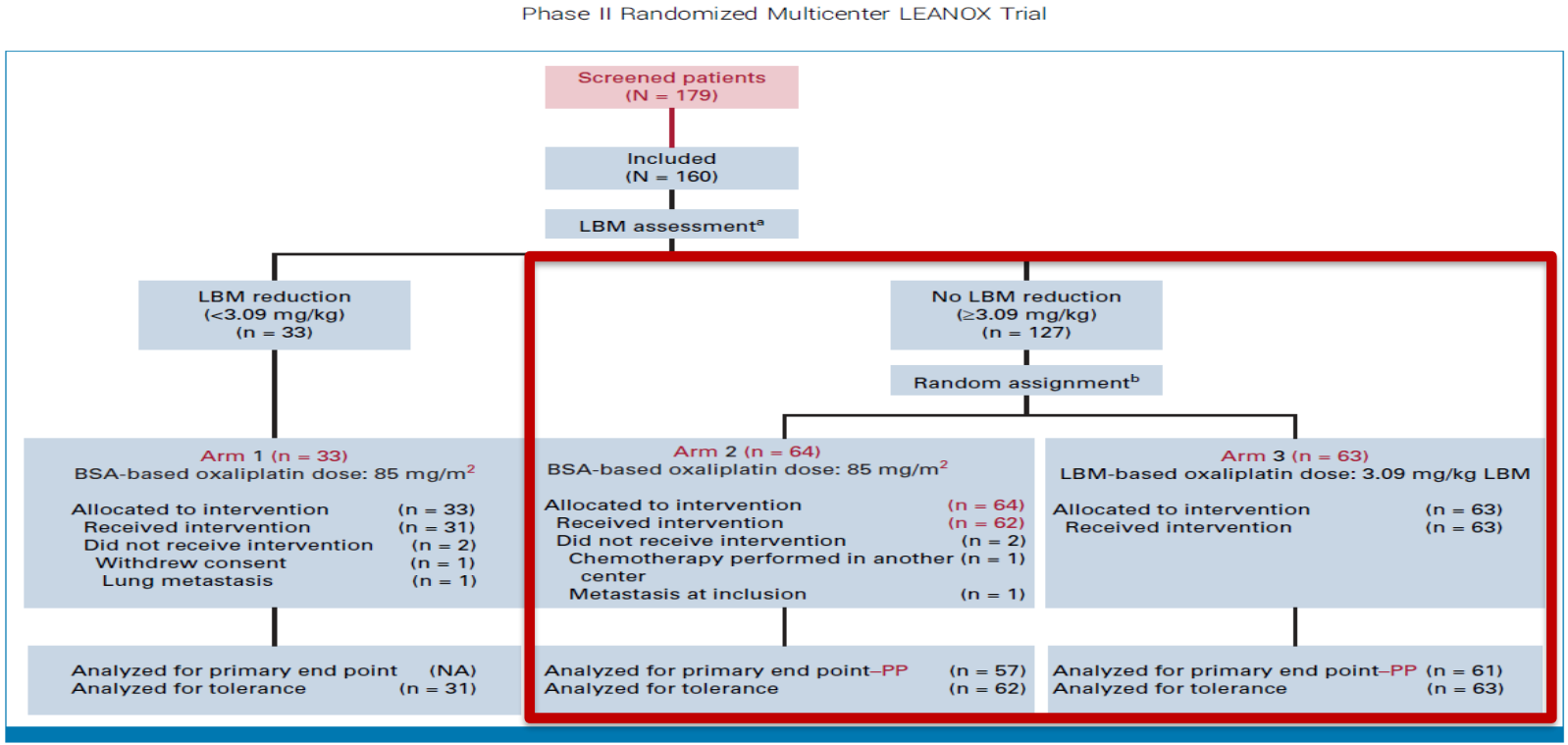
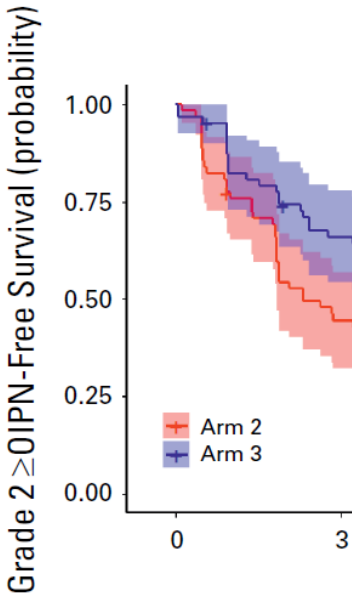
S Gérard et al. Body Composition and Anti-Neoplastic Treatment in Adult and Older Subjects - A Systematic Review. J Nutr Health Aging 2016;20(8):878-888.

DOSIFICACION – COMPOSICIÓN CORPORAL



Eric Assenat et al. Impact of Lean Body Mass-Based Oxaliplatin Dose Calculation on Neurotoxicity in Adjuvant Treatment of Stage III Colon Cancer: Results of the Phase II Randomized LEANOX Trial. J Clin Oncol.2025 Aug 10;43(23):2616-2627

DOSIFICACION – COMPOSICIÓN CORPORAL (TOXICIDAD)



OIPN Characteristic	Arm 1 (n = 33)	Arm 2 (n = 62)	Arm 3 (n = 63)	Total (N = 156)	*P*
Primary end point (per-protocol population)					
No.	NA	57	61	118	
Patients without grade ≥2 OIPN during the first six cycles, No. (%)	NA	24 (42.1)	41 (67.2)	NA	.01[a]
Secondary end points (safety population)					
Time to onset of the first grade ≥2 OIPN, months					
Median (95% CI)	4.1 (3.1 to NA)	2.3 (1.8 to 4.6)	5.7 (4.4 to NA)	4.3 (3.1 to 5.7)	.01[b]
Patients with at least one grade ≥2 OIPN during treatment, No. (%)					.01[a]
No	13 (41.9)	20 (32.3)	34 (54)	67 (43)	
Yes	18 (58.1)	42 (67.7)	29 (46)	89 (57.1)	
Patients with at least one grade ≥2 OIPN after treatment, No. (%)					.19[a]
No	22 (71)	44 (71)	51 (81)	117 (75)	
Yes	9 (29)	18 (29)	12 (19.1)	39 (25)	

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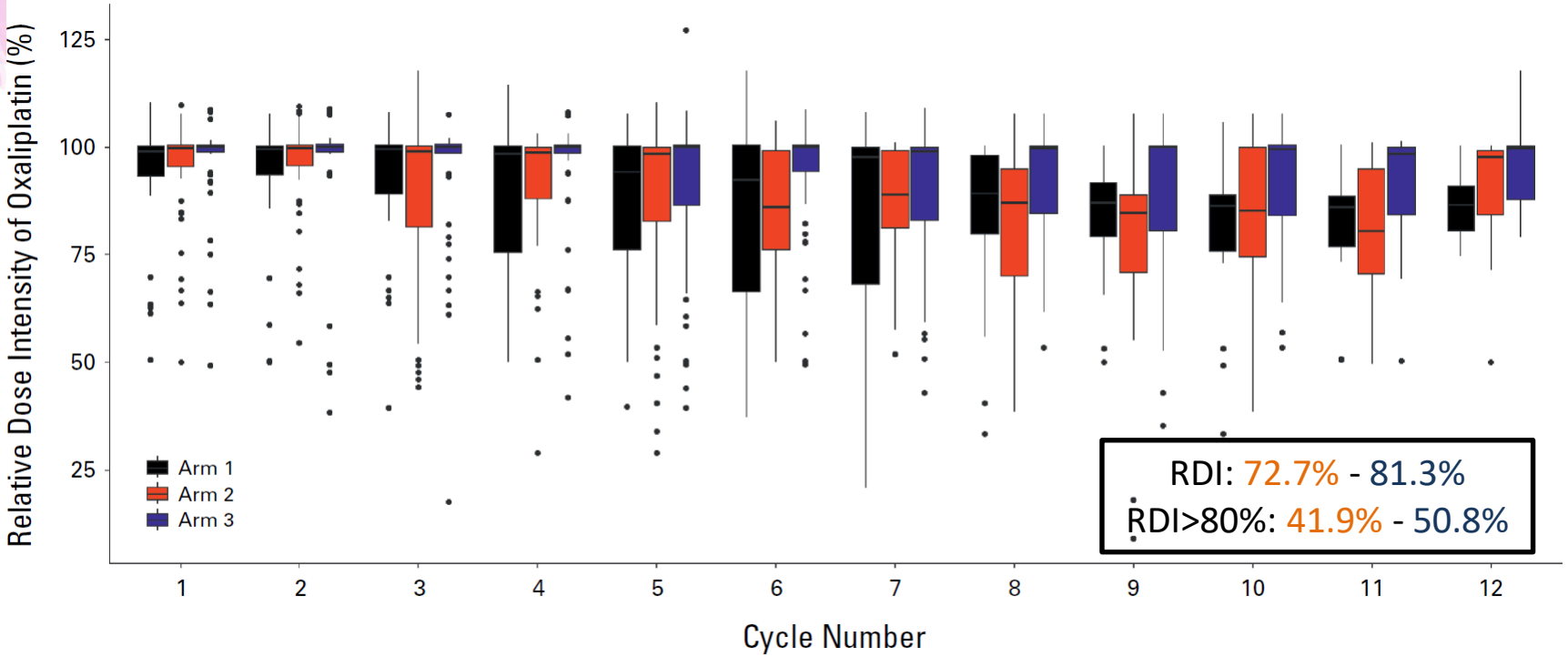
Eric Assenat et al. Impact of Lean Body Mass-Based Oxaliplatin Dose Calculation on Neurotoxicity in Adjuvant Treatment of Stage III Colon Cancer: Results of the Phase II Randomized LEANOX Trial. J Clin Oncol.2025 Aug 10;43(23):2616-2627

DOSIFICACION – COMPOSICIÓN CORPORAL



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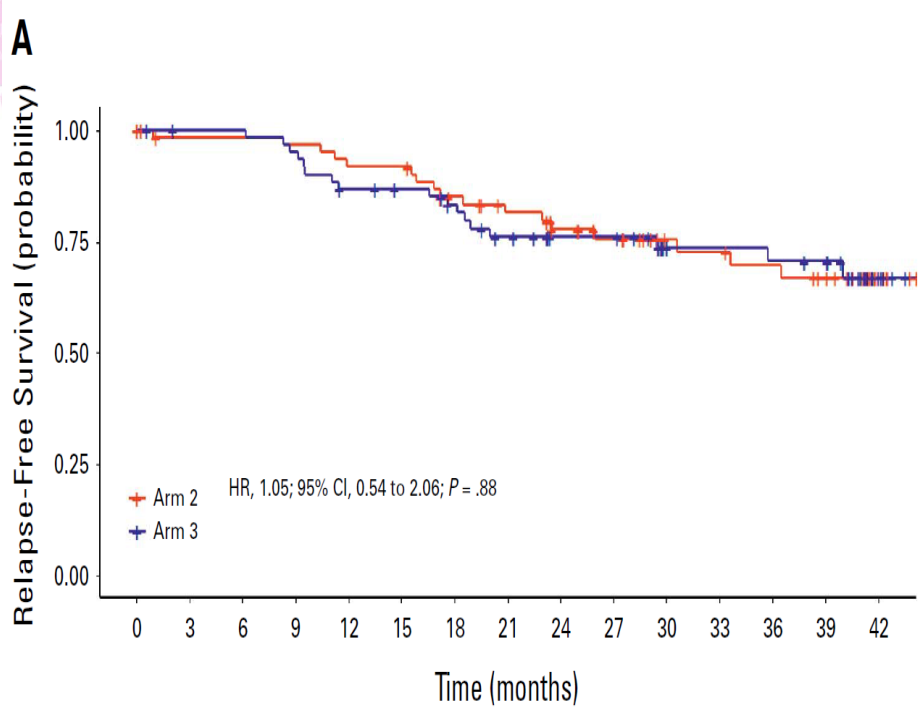
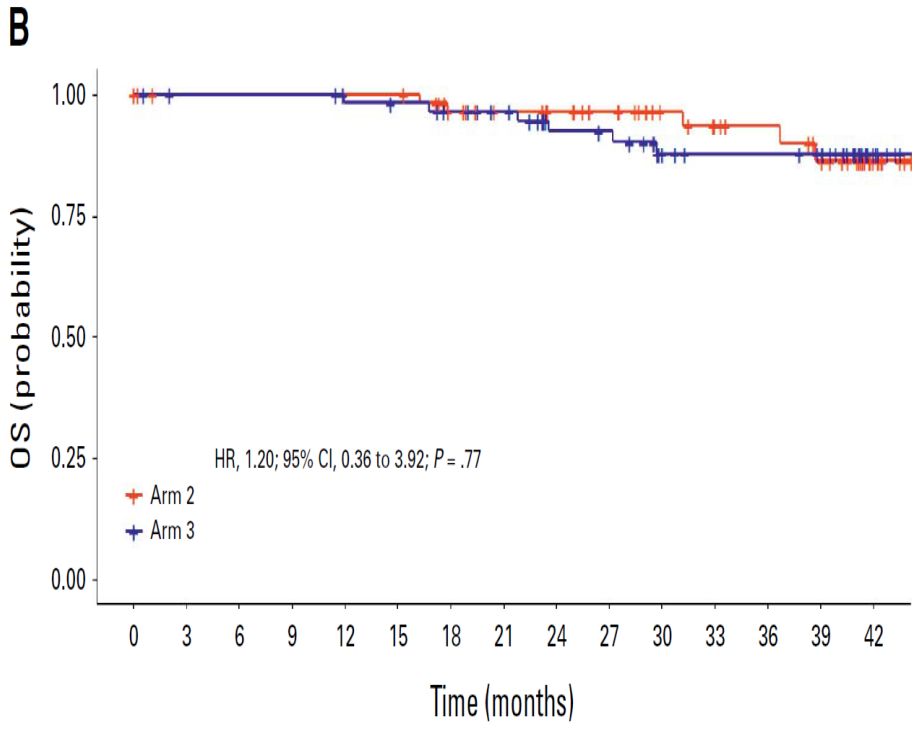
Eric Assenat et al. Impact of Lean Body Mass-Based Oxaliplatin Dose Calculation on Neurotoxicity in Adjuvant Treatment of Stage III Colon Cancer: Results of the Phase II Randomized LEANOX Trial. J Clin Oncol.2025 Aug 10;43(23):2616-2627

EFECTIVIDAD – BSA vs LBM





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INTERACCIONES FARMACOLÓGICAS

Table 2
Summary of principal DDIs for oncological drugs belonging to CDK4/6i, PARPi, ARTA, ADC class.

			CDK4/6i			PARPi				ARTA				ADC			
			Abema-ciclib	Palbo-ciclib	Ribo-ciclib	Nira - parib	Ola-parib	Ruca-parib	Talazo-parib	Abira-terone	Apalu-tamide	Darolu-tamide	Enzalu-tamide	T-DXd	TDM-1	Enfort-umab	SG
INH	Strong	2C9															
		2C19															
		2C8									*		*				
		2D6															
		3A4	*	*	*		*				*	*					
		UGT															
		BCRP															
		OATP															
		Pg-P							*			*					
	Mode-rate	2C9															
		2C19															
		2C8															
		2D6															
		3A4					*										
		UGT															
		BCRP															
		OATP															
		Pg-P															
IND		2C9															
		2C19															
		2C8															
		2D6															
		3A4										#					
		UGT															
		BCRP															
		OATP															
		Pg-P										#					
Sub-strate		2C9						*			#		*				
		2C19									#		*				
		2C8															
		1A2						*									
		2B6									*		*				
		2D6															
		3A4						*			#		*				
		UGT									*		*				
		BCRP									*						
		OATP									*						
		Pg-P									*		*				

Legend
RED: Concomitant use should be avoided.
ORANGE: Caution is advised in case of concomitant use.
GREEN: No risk of interaction.
PINK: No data available, or no formal interaction studies performed.

Media = 4 (1 – 15)

40-50%

Fiorenza Santamaria et al. Clinical implications of the Drug-Drug Interaction in Cancer Patients treated with innovative oncological treatments. Crit Rev Oncol Hematol. 2024 Aug:200_104405

Justin J Cheng et al. Polypharmacy in Oncology. Clin Geriatr Med 2022 Nov;38(4):705-714.

PK – EFECTIVIDAD/SEGURIDAD

Table 1 Evidence for TDM for targeted oral antineoplastic drugs

Evidence level	Recommendation	Description
1	Strongly recommended	Randomised, prospective studies demonstrated positive effect of routine TDM with regards to efficacy and/or safety.
2	Recommended	There is an established exposure-response relationship using standard dosage from retrospective studies, a target is established **and** a feasibility study has been performed.
3	Potentially useful	An exposure-response or exposure-safety relationship using standard dosage has been identified and a potential target has been reported.
4	Exploratory	An exposure-response or exposure-safety relationship using standard dosage has been identified but no target has been reported.
5	Not recommended	No exposure-response or exposure-safety relationship using standard dosage has been identified **and/or** - there is very few data on pharmacokinetics of the drug; - there are more useful targets than plasma concentration (PD); - there is evidence that TDM is not useful

Fármaco	Relación	Cmin
Abiraterona	Efectividad	≥ 8,4ng/ml
Everolimus	Efectividad	≥ 10ng/ml
Imatinib	Efectividad (LMC)	≥ 1000ng/ml
	Efectividad (GIST)	≥ 1100ng/ml
Pazopanib	Efectividad	≥ 20,5mg/L
	Seguridad	≤46mg/L
Sunitinib	Efectividad	≥ 50ng/ml
	Seguridad	≤87,5ng/ml
Tamoxifeno	Efectividad	≥ 5,97g/ml
Trametinib	Efectividad	≥ 10,6ng/ml

Fármaco	Relación	Cmin
Afatinib	Seguridad	≤ 28,5 ng/ml
Alectinib	Efectividad	≥ 435ng/ml
Cabozantinib	Efectividad	≥ 537ng/ml
	Seguridad	≤ 618 ng/ml
Crizotinib	Efectividad	≥ 235ng/ml
Dasatinib	Seguridad	≤ 2,5 ng/ml
Lenvatinib	Seguridad	≤88 ng/ml
Nilotinib	Efectividad	≥ 469ng/ml
Olaparib	Seguridad	≤2500ng/ml
Osimertinib	Seguridad	≤259ng/ml
Regorafenib	Efectividad	≥ 2900ng/ml
	Seguridad	≤4300ng/ml
Vemurafenib	Efectividad	≥ 50ng/ml

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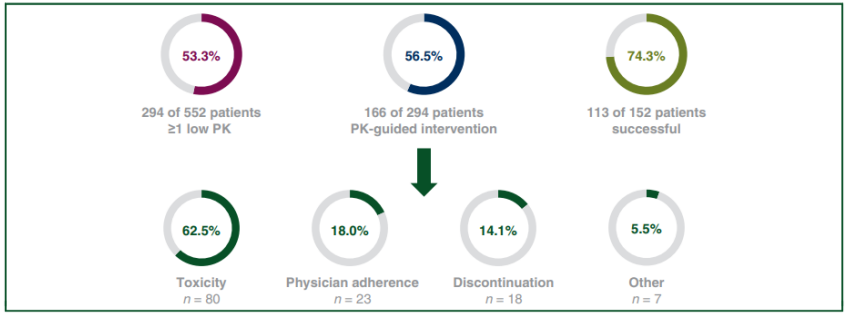
Anna Mueller-Schoell et al. Therapeutic drug monitoring of oral targeted antineoplastic drugs. Eur J Clin Pharmacol. 2021 Apr;77(4):441-464
Van der Kliej et al. Therapeutic Drug Monitoring of Kinase Inhibitors in Oncology. Clin Pharmacokinet. 2023 Oct;62(10):1033-1064

MONITORIZACIÓN Y PERSONALIZACIÓN



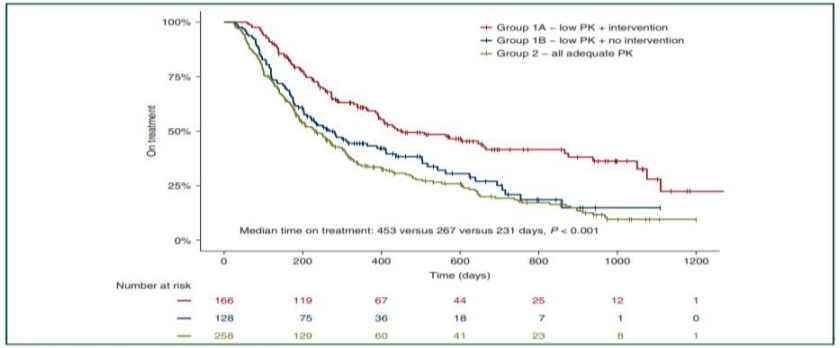
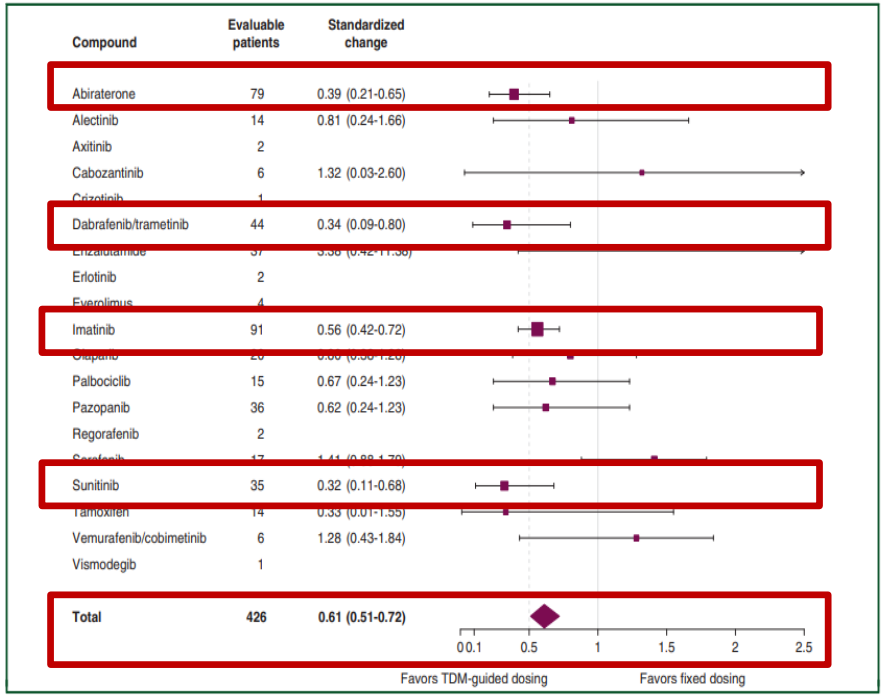


Figure 5. Kaplan–Meier curve of time on treatment.
Group 1A are patients with one or more PK samples below the target who received a pharmacokinetically guided intervention. Group 1B are patients with one or more PK samples below the target who did not receive a pharmacokinetically guided intervention due to various reasons (i.e. toxicity, physician adherence, treatment discontinuation). Group 2 are patients with all PK samples above the target.
PK, pharmacokinetic.



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SL Groenland et al. Therapeutic drug monitoring-based precision dosing of oral targeted therapies in oncology: a prospective multicenter study. Ann Oncol. 2022 Oct;33(10):1071-1082

¿POR DONDE EMPEZAMOS?

Table 1 Calculation of the score

	Score	Variable	Modality associated	Score value (/100)
Interpatient pharmacokinetic variability (i)	Variability (0–25)	Food score ratio AUC fed-fasted (r) ratio AUC high fat meal-fasted (r)	No interaction: $r<1.25$	0
			Mild interaction: $1.25<r\leq2.5$	1
			Moderate interaction: $2.5<r\leq5$	2
			Strong: $r>5$	2.5
		PPI score decrease of AUC with the addition of PPI	No interaction: decrease of AUC<20%	0
			Mild interaction: 20%≤decrease of AUC ≤40%	1
			Moderate interaction: decrease of AUC>40%	2.5
		CV score	CV AUC/5	0–20
Feasible dose-adaptation strategy (ii)	Technical complexity (0–15)	PK linearity	Absence of PK linearity	0
			PK linearity at recommended doses	5
		Active metabolite	Existence of active metabolite	0
			Absence of active metabolite	5
		Half-life	<12 hours	0
			≥12 hours	5
Exposure-efficacy relationship (iiia)	Efficacy (0–40)	ERR	Overall ERR	10
			OS ERR	10
			PFS ERR	10
			ORR ERR	10
Exposure-safety relationship (iiib)	Safety (0–20)	MTD phase 1	Absence of MTD	0
			Existence of MTD	10
		ESR	Toxicity with ESR	No modifications
			Toxicity without ESR	10−(number of toxities without ESR×2.5)
	Final score = variability score + technical complexity score + efficacy score + safety score			

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Arthur Géraud et al. A Score to Predict the Clinical Usefulness of Therapeutic Drug Monitoring: Application to Oral Molecular Targeted Therapies in Cancer. Clin Pharmacol Ther. 2024 Sep;116(3):678-689

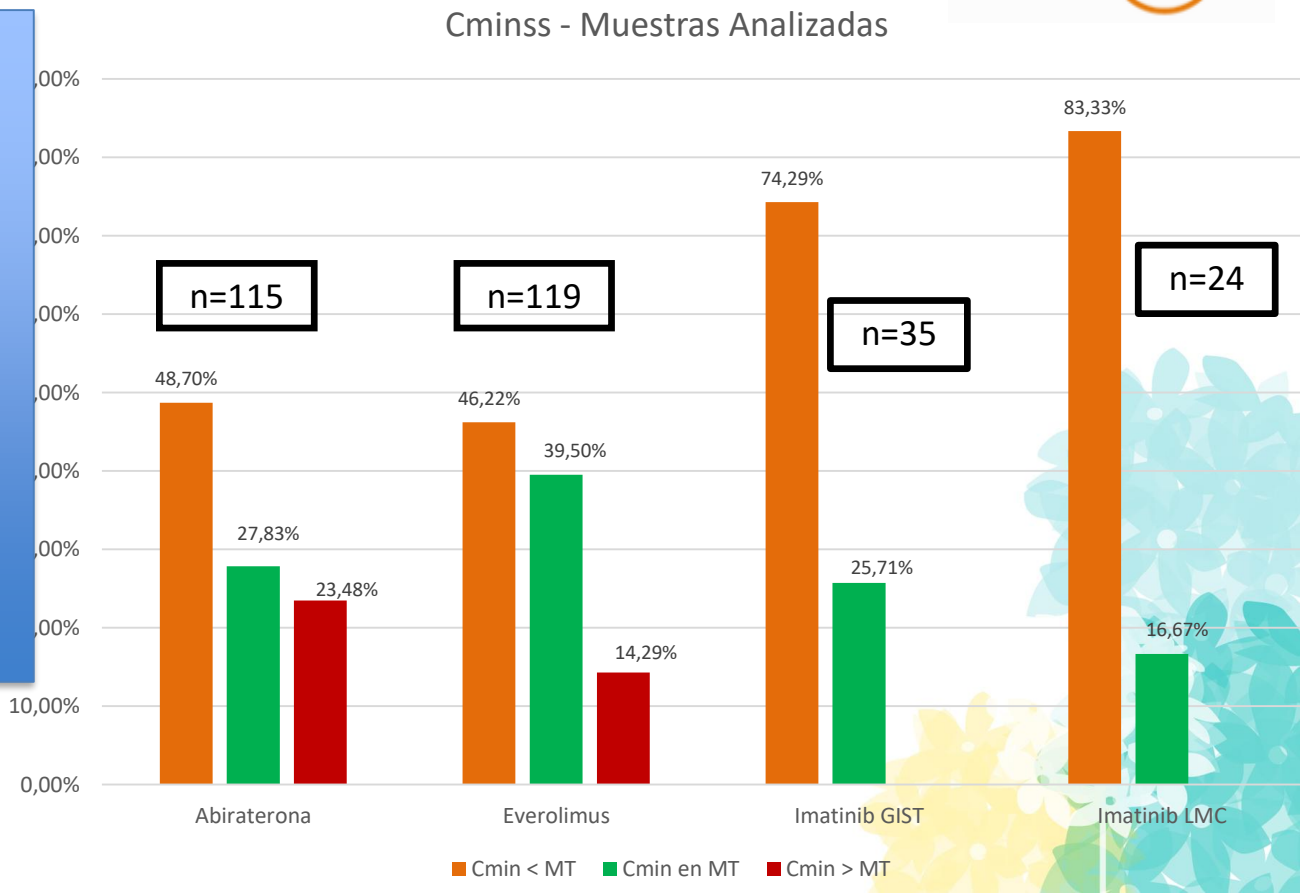
PROYECTO DIANA (ICO)

Abiraterona: 24.7ng/ml (0.6 -99.9ng/ml)

Imatinib GIST: 987.2ng/ml (241.1 – 2526.8 ng/ml)

Imatinib LMC: 815.5ng/ml (289.9 – 2306.9)

Everolimus: 14.47 ng/ml (2.06 – 72.97)



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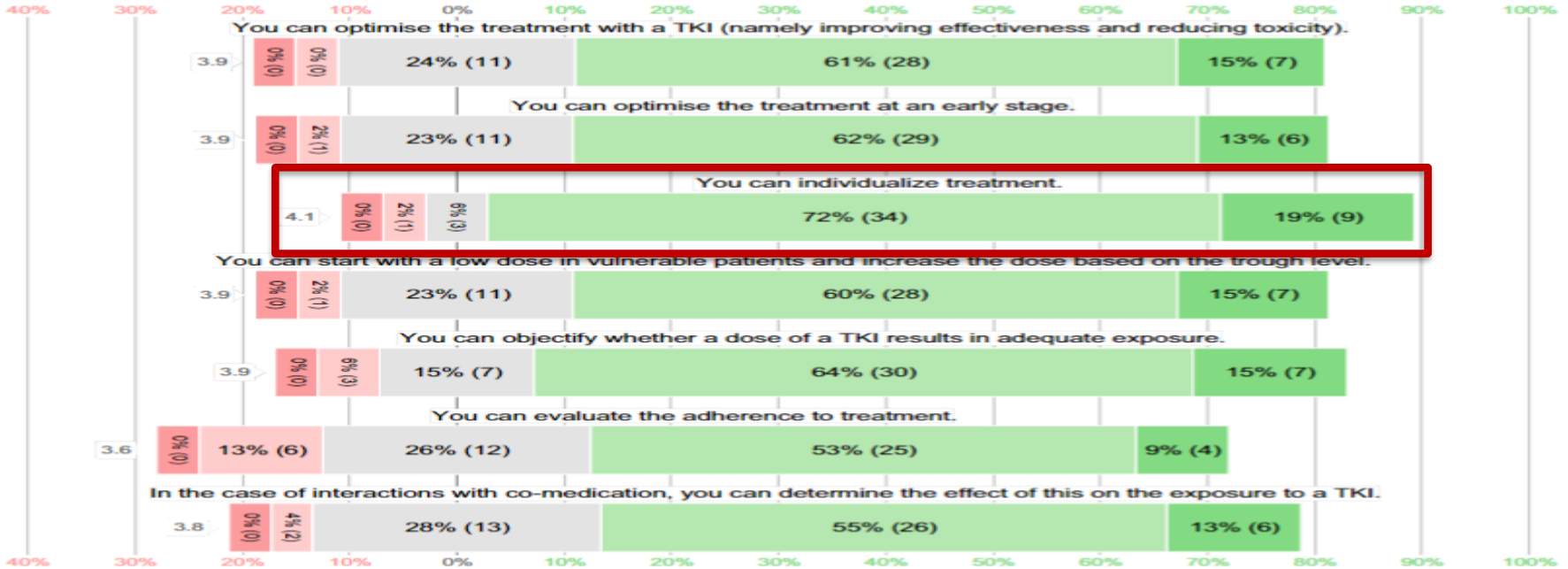
ONCOLOGIA OPINION TDM



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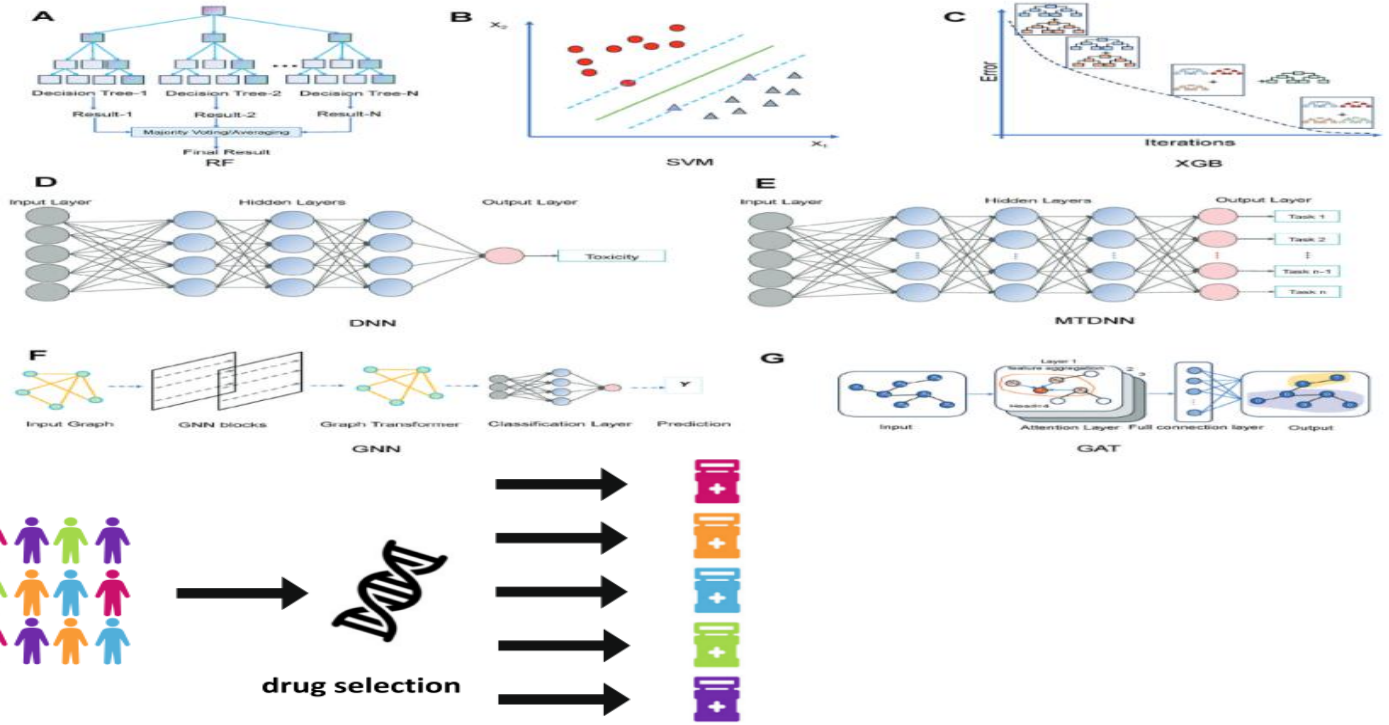
Alexandra Flynn [1], Peter Galettis [1], Howard Gurney [2], Michael Michael [3], Ingrid Desar [4], Kim Westerdijk [4], Jennifer Schneider [1], Jennifer Martin [1]. Therapeutic drug monitoring in anticancer agents: perspectives of Australian medical oncologists. Intern Med J. 2024 May 20. doi: 10,1111/imj.16415

INTELIGENCIA ARTIFICIAL



[Changsen Bai](#) et al. Machine Learning-Enabled Drug-Induced Toxicity Prediction.Adv Sci /Whein). 2025 Feb 3: e2413405.

PROYECTO DIANA-1

Cminss
15,3ng/ml
+ HMZ PIK3R1

STOP

10mg/12h
Cminss=8,7-10,6ng/ml

Cminss
3,6ng/ml

2 FÁRMACOS
+ CYP3A4

EVEROLIMUS
10mg/dia

Cminss
37,1 ng/ml

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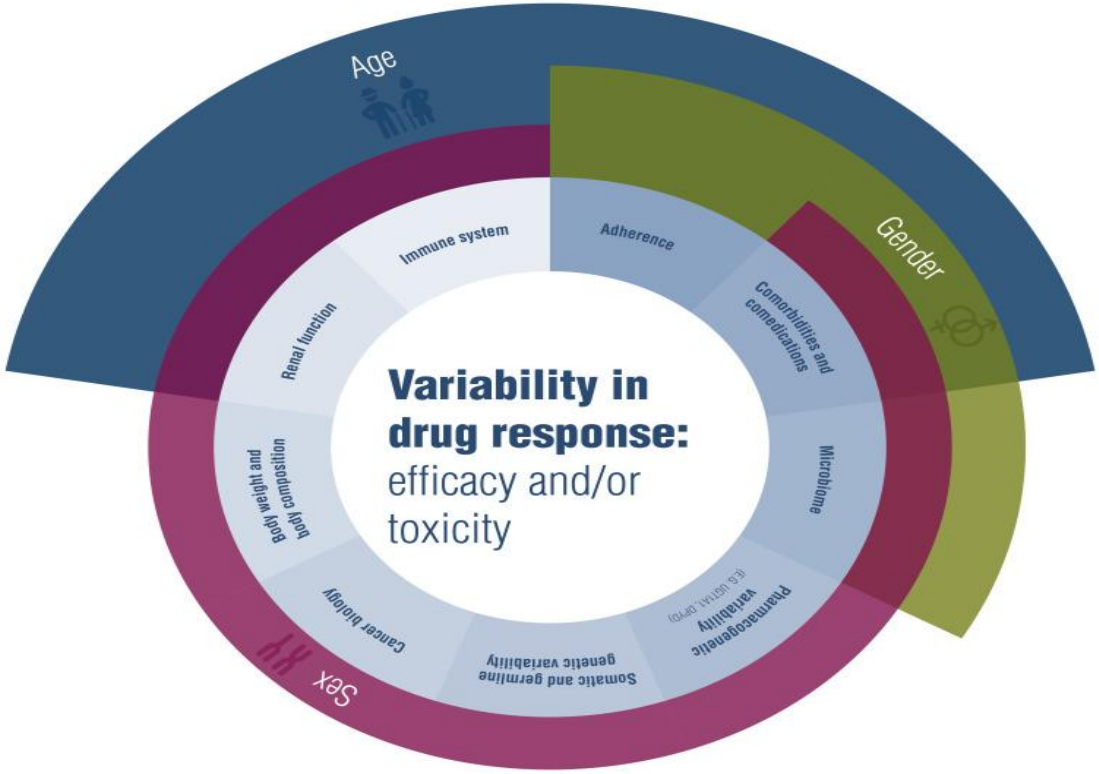
CONCLUSIONES



J Delahousse et al. Sex differences in the pharmacokinetics of anticancer drugs: a systematic review. ESMO OPEN. 2024 Dec 19; 9(12):104002

Sapere Aude Reflexión ante nuevos retos

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sefh Sociedad Española de Farmacia Hospitalaria

Gracias

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