

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Ramon y Cajal University Hospital standard rapid oral desensitization protocol adapted for total dose of elexacaftor 100mg / Tezacaftor 50mg / Ivacaftor 75mg. Total time: 160 min (2.40h), plus observation. Based on dose of elexacaftor (100 mg). Suspension stability was 24 hours delimited.

Drug	OraSweet®/Oraplus® suspension	Suspension concentration (mg/ml)
ELX/TEZ/IVA	Suspension A	1 mg/ml
ELX/TEZ/IVA	Suspension B	10 mg/ml

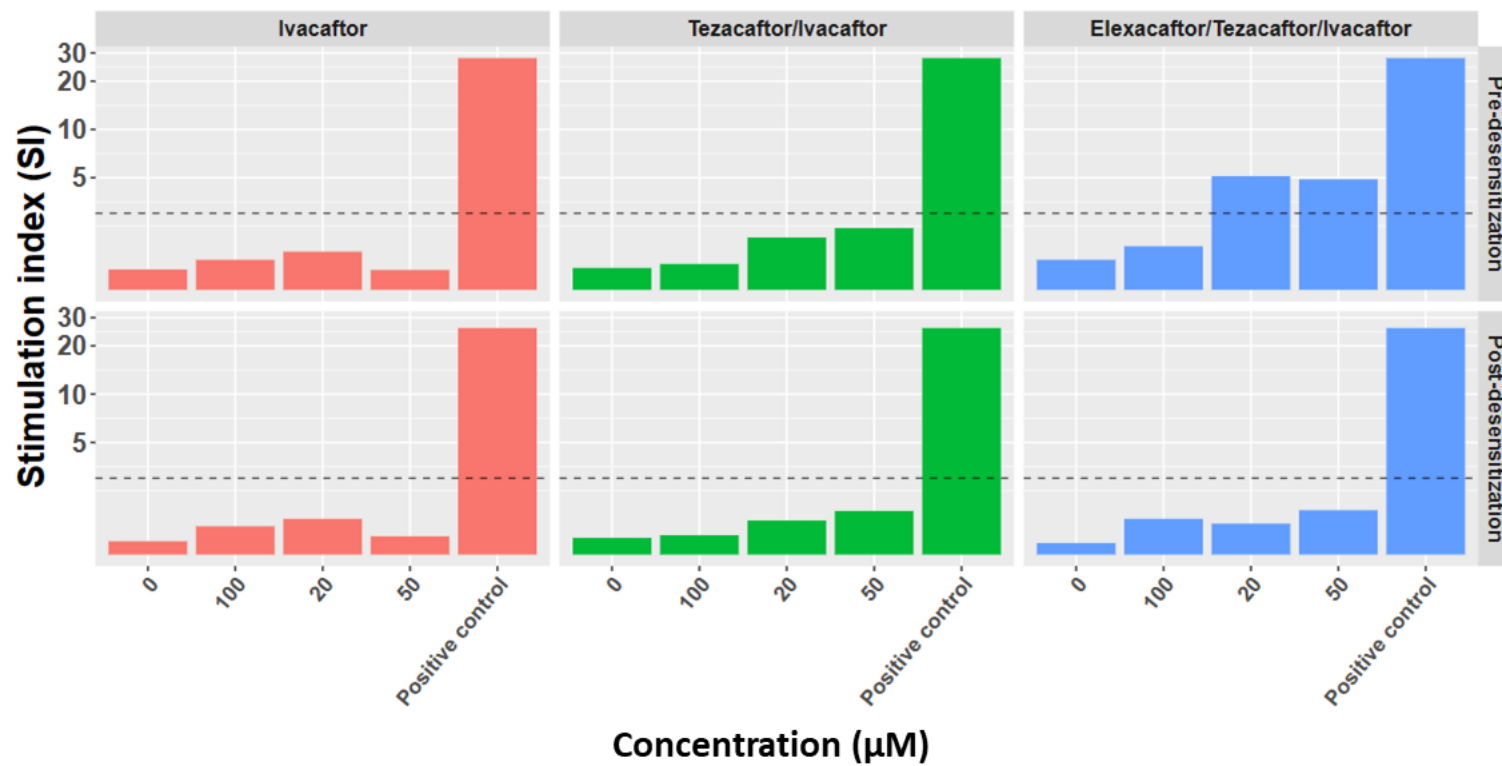
Step	Suspension	Administered volumen, ml	Interval, min	Administered dose, mg	Fold increase per-step	Approximative cumulative dose, mg
1	A	1	20	1		1
2	A	2	20	2	X2	3
3	A	3	20	3	X1,5	6
4	B	0,5	20	5	X1.6	10.5
5	B	0,7	20	7	X1.4	17.5
6	B	1	20	10	X1.4	28
7	B	1,6	20	16	X1.6	44

8	B	2,4	20	24	X1.5	68
9	B	3,2	120 (observation)	32	X1.4	100

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Supplementary Figure 1. Cell proliferative response before and after desensitization with ELX/TEZ/IVA. Charts reflect cell SI according to drug concentration in LTTs. Upper images show IVA, TEZ/IVA and ELX/TEZ/IVA LTT results before desensitization in this patient. Lower images show LTT results after desensitization. An SI greater than 3 is considered positive; weakly positive is between 2 and 3. Cells were also stimulated with Dynabeads CD3/CD28 (Thermo Fisher Scientific, Madrid, Spain; CD3/CD28, 1 mL/well) as a positive control.

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