

Convegno ECM

CARCINOMA MAMMARIO

FARMACI ANTITUMORALI ORALI E
SOTTOCUTE: IMPATTO SULLA QUALITÀ
DI VITA DEI PAZIENTI
E SULL'ORGANIZZAZIONE

Verona
24 ottobre
2025

Sala Industria
Camera di Commercio di Verona

Coordinatori scientifici:
Stefania Gori
Roberto Tessari

Con il Patrocinio di



**II SESSIONE: FORMULAZIONI SOTTOCUTE DI TRASTUZUMAB
E PERTUZUMAB: ORGANIZZAZIONE E GESTIONE DEI PAZIENTI**

Moderatori: *Chiara Alberti, Laura Merlini*

**Trastuzumab e pertuzumab sottocute nelle forme HER2+
e atezolizumab sottocute nelle forme TN: i dati della letteratura.**

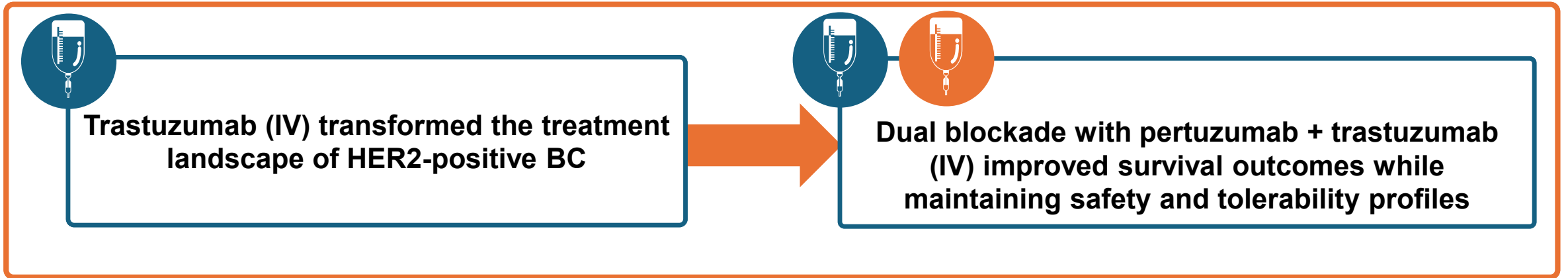
Alessandra Modena

UOC Oncologia Medica

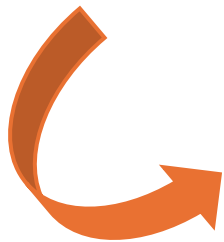
IRCCS Ospedale Sacro Cuore Don Calabria di Negrar

SC Trastuzumab e pertuzumab formulations in HER2+ BC

Background (1)



- HER2 overexpression occurs in about 15-20% of BC and is associated with *high disease recurrence* and *short survival*.
- Combining IV pertuzumab with trastuzumab and chemotherapy for patients with HER2-positive BC led to *significantly improved overall survival* in CLEOPATRA (metastatic setting), *improved pCR rates* in NeoSphere (neoadjuvant setting) and a *clinically meaningful improvement in invasive disease-free survival* in patients at high risk of recurrence in APHINITY (adjuvant curative setting).



Pertuzumab + trastuzumab and chemotherapy is standard treatment for patients with HER2-positive early and metastatic BC.

Background (2)

- Despite their clinical benefits, they are infused sequentially over a long time → repeated invasive IV treatment can be *inconvenient and painful for patients*
- Total administration time can amount to several hours, which places a *burden on patients and healthcare system*



**Development of a fixed-dose subcutaneous formulations,
irrespective of patient weight or age**



The SC formulations contain the same two mAbs as approved for IV pertuzumab and trastuzumab, but have a **different route** of administration (one syringe for SC injection) → **less invasive**.



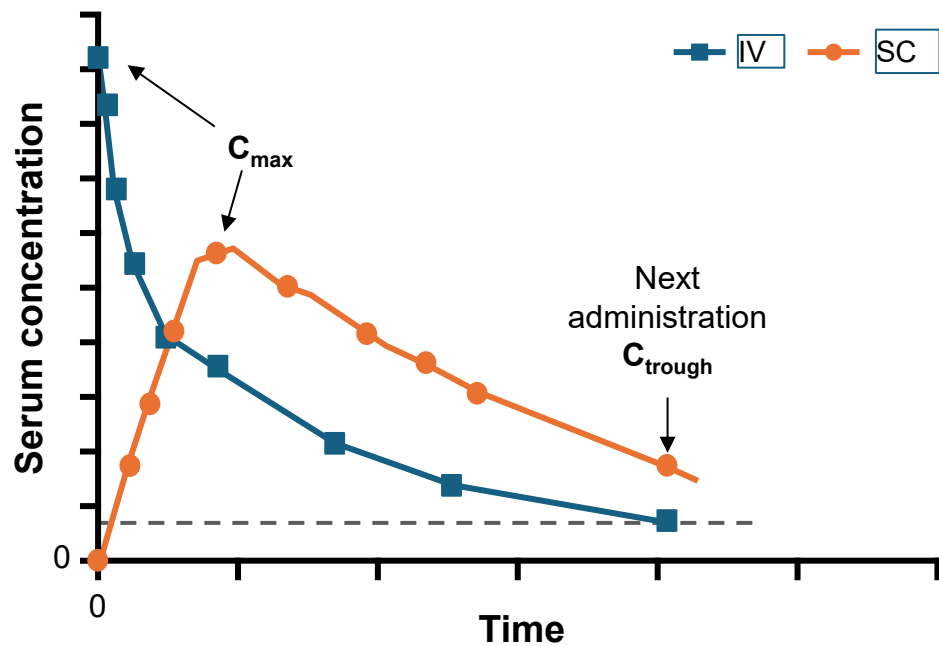
They are formulated with 2000 U/mL recombinant human hyaluronidase (rHuPH20) to allow SC administration of **higher drug volumes** (1200 mg pertuzumab, 600 mg trastuzumab, 15 mL loading dose; 600 mg pertuzumab and trastuzumab, 10 mL maintenance dose).



They are a ready-to-use fixed-dose formulations, administered by a SC injection **over 8-5 minutes** and with short observation times (30-15 minutes) → **faster**.

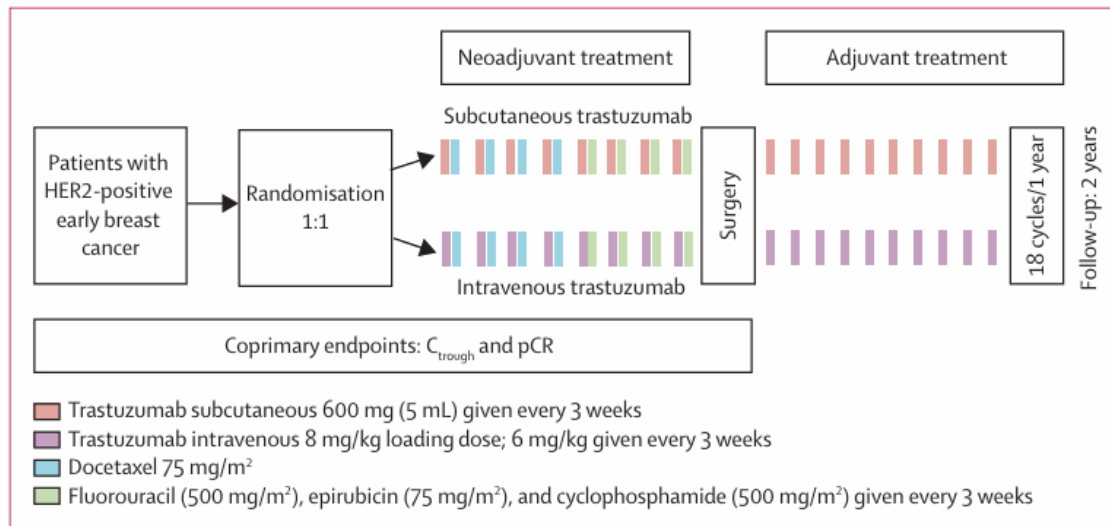
PK endpoints are a key focus of fixed-dose SC formulation clinical development programme and are used to assess bioequivalence between IV and SC formulations

Plasma/serum concentration–time curve*

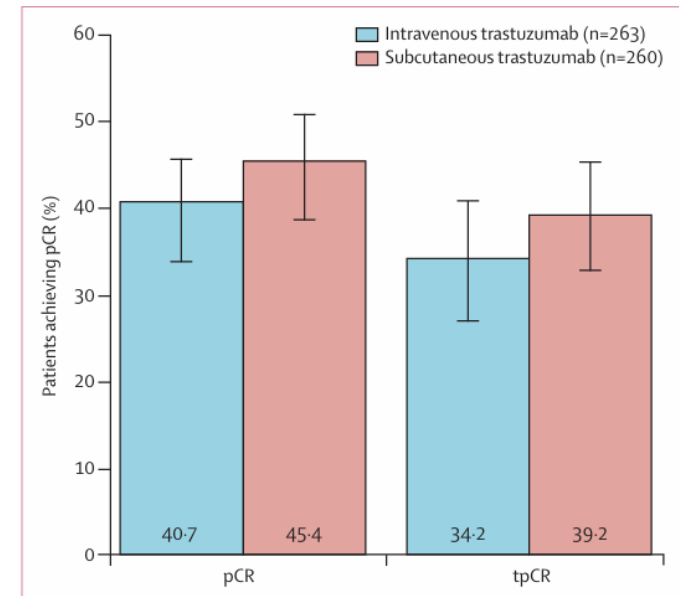


- **C_{trough}** = Trough plasma/serum drug concentration; the concentration measured at the end of a dosing interval
 - Related to mode of action
 - Associated with clinical outcomes
- **AUC** = Area under the plasma/serum concentration–time curve;
 - Provides exposure information over the course of the treatment cycle (how much of a drug stays in the body and for how long)
 - May correlate with C_{trough}
- **C_{max}** = Maximum (peak) plasma/serum drug concentration
 - C_{max} after IV is not subject to distribution and elimination effects, compared with C_{max} after SC which requires time for absorption and is subject to elimination effects before reaching the bloodstream
 - Not clearly correlated with clinical outcomes

Trastuzumab SC: *HannaH trial*



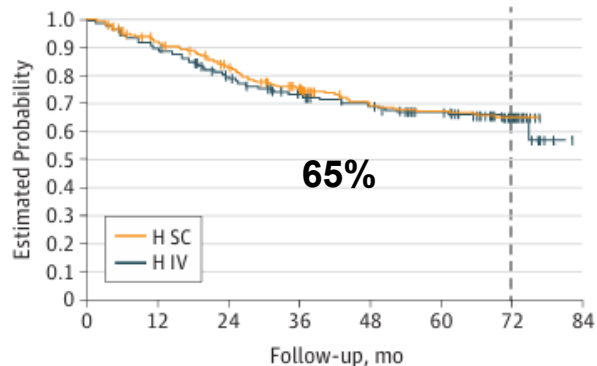
	Intravenous trastuzumab (n=235)	Subcutaneous trastuzumab (n=234)
Primary pharmacokinetic endpoint		
C_{trough} predose cycle 8		
Mean (µg/mL; SD)	57.8 (30.3)	78.7 (43.9)
Geometric mean (µg/mL; percentage coefficient of variation)*	51.8 (52.5%)	69.0 (55.8%)



SC trastuzumab has a pharmacokinetic profile and efficacy non-inferior to standard IV administration, with a similar safety profile

HannaH trial: final analysis at a mFU of 6 ys

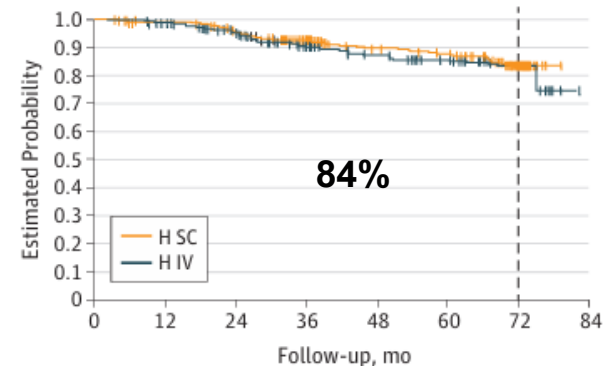
A EFS by study group



No. at risk	0	12	24	36	48	60	72	84
H SC	294	264	231	202	171	163	86	0
H IV	297	263	224	200	181	169	103	0

HR, 0.98 (95% CI, 0.74-1.29)

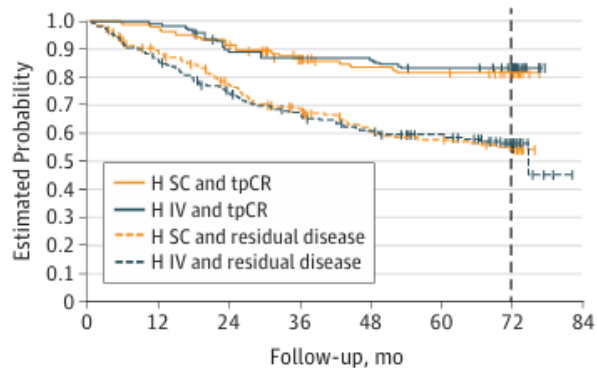
B OS by study group



No. at risk	0	12	24	36	48	60	72	84
H SC	294	283	265	229	200	193	98	0
H IV	297	289	265	225	205	193	115	0

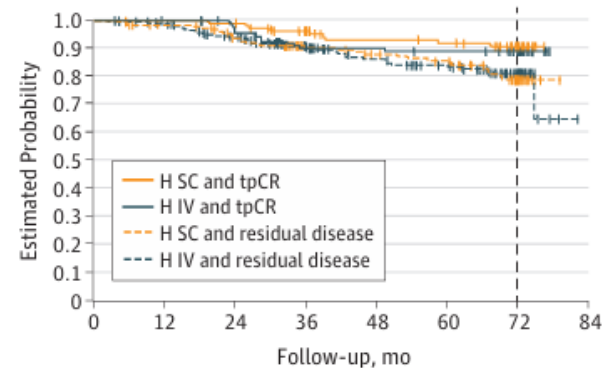
HR, 0.94 (95% CI, 0.61-1.45)

C EFS by tpCR status



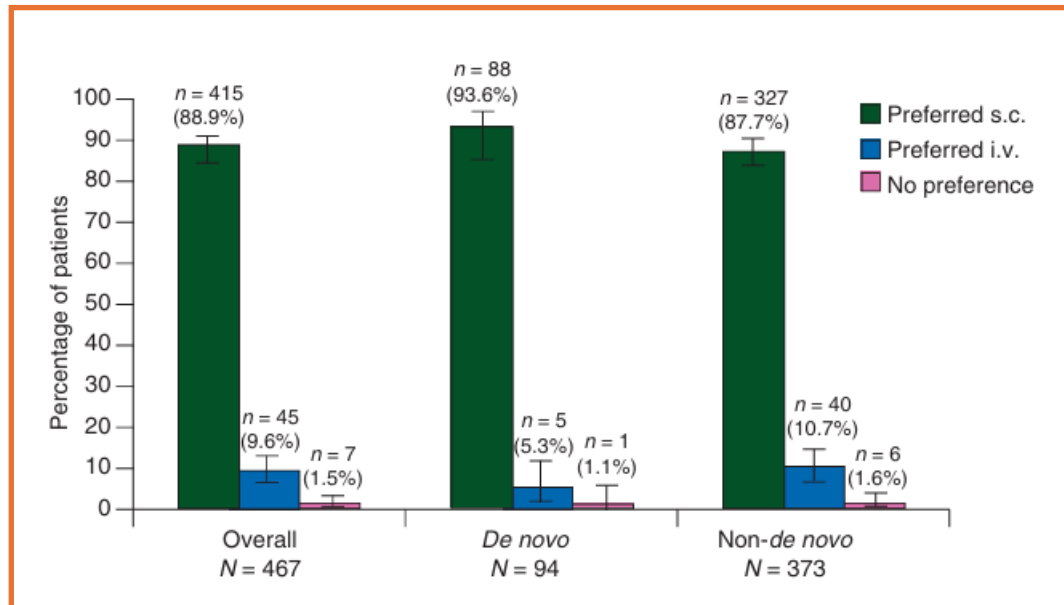
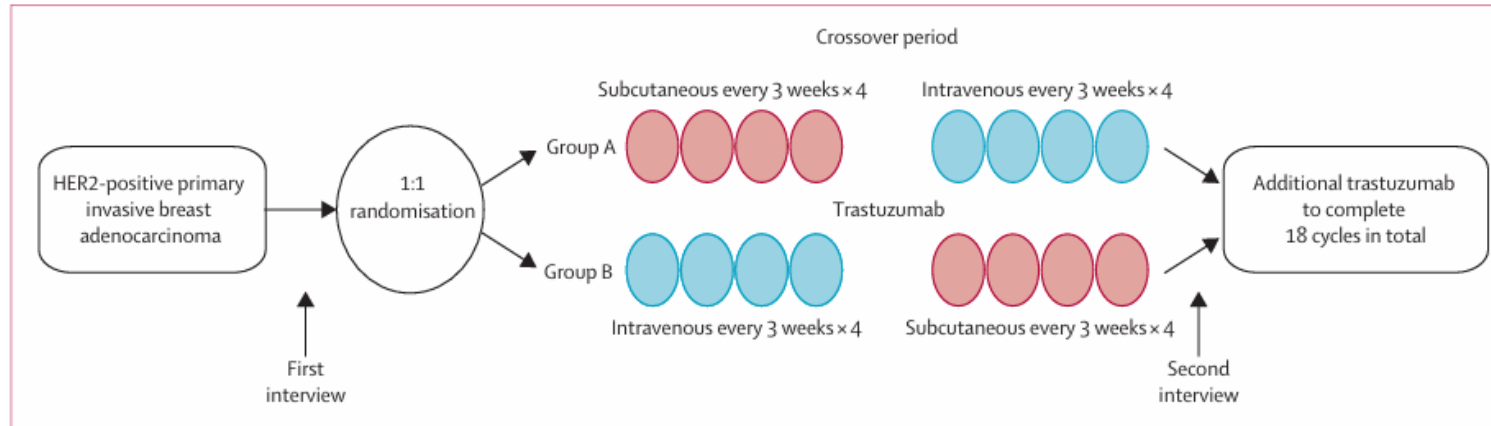
H SC and tpCR 6-y EFS, 82% (95% CI, 74%-89%)
 H SC and residual disease 6-y EFS, 54% (95% CI, 47%-62%)
 H IV and tpCR 6-y EFS, 83% (95% CI, 76%-91%)
 H IV and residual disease 6-y EFS, 57% (95% CI, 49%-64%)

D OS by tpCR status



H SC and tpCR 6-y OS, 91% (95% CI, 85%-97%)
 H SC and residual disease 6-y OS, 79% (95% CI, 72%-86%)
 H IV and tpCR 6-y OS, 89% (95% CI, 82%-95%)
 H IV and residual disease 6-y OS, 81% (95% CI, 75%-87%)

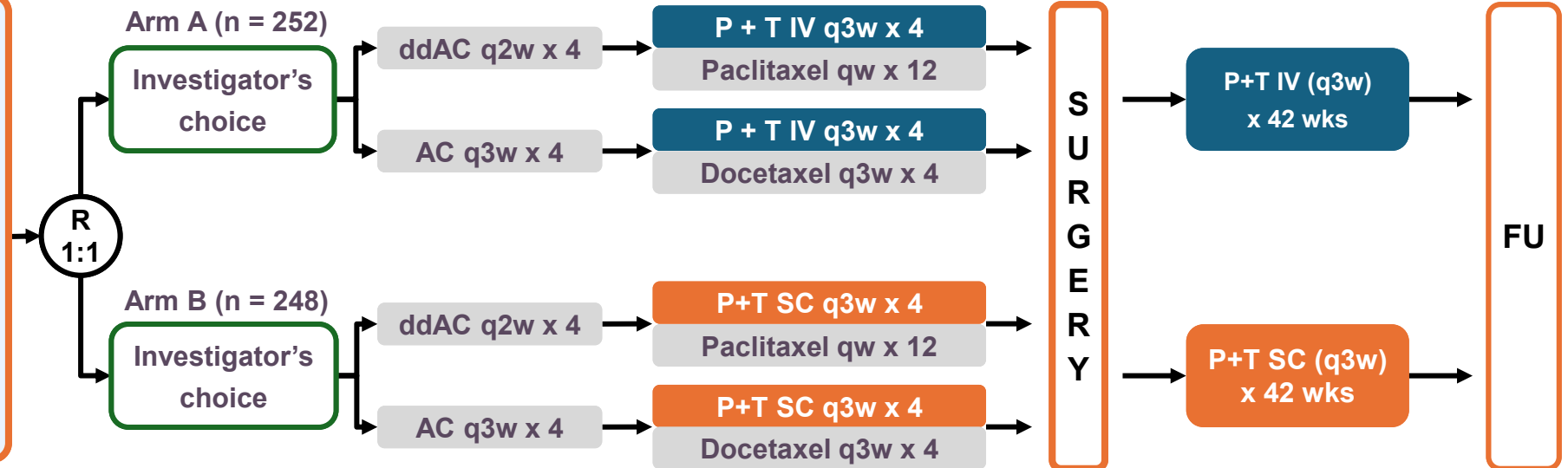
Patient preference administration: PrefHer trial



	n*
Subcutaneous preferred, n=216	
Time saving	195
Less pain/discomfort	88
Convenience to patient	35
Ease of administration	33
Problems with intravenous	25
Less stress/anxiety	15
Other	6
Intravenous preferred, n=16	
Fewer reactions (less pain, bruising, irritation, etc)	11
Other	5
Environment/staff	2
Perceived efficacy	1
Ecological considerations	1

PERTUZUMAB + TRASTUZUMAB SC: FeDeriCa trial

Patients with centrally confirmed operable or locally advanced/ inflammatory HER2-positive BC (with primary tumour >2 cm or node-positive) Stage II–IIIC. Left ventricular ejection fraction $\geq 55\%$. (N = 500)

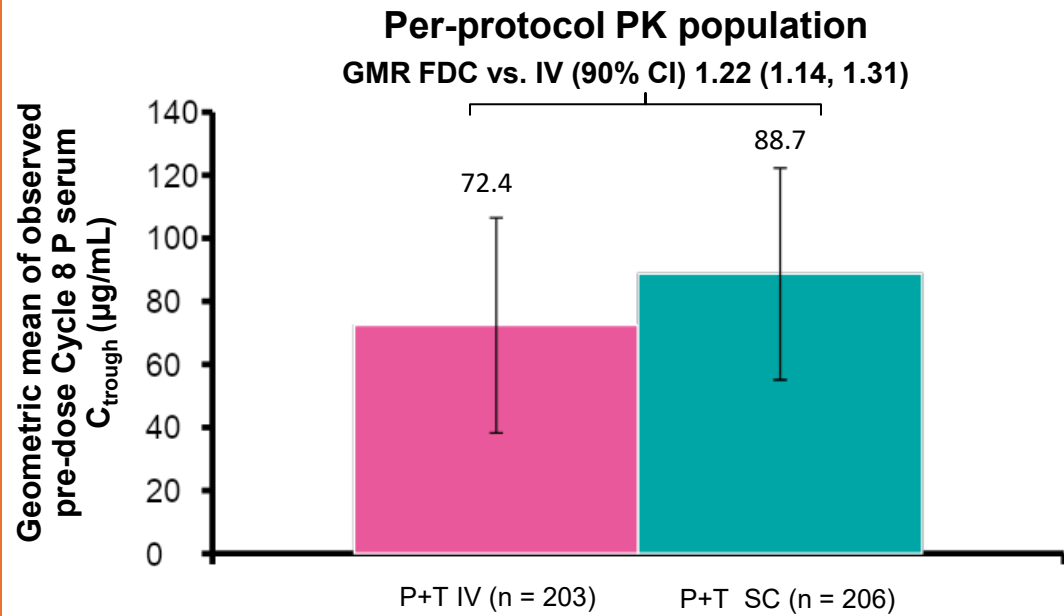


Stratification factors: Hormone receptor status; clinical stage at presentation (Stage II–IIIA or IIIB–IIIC); type of chemotherapy

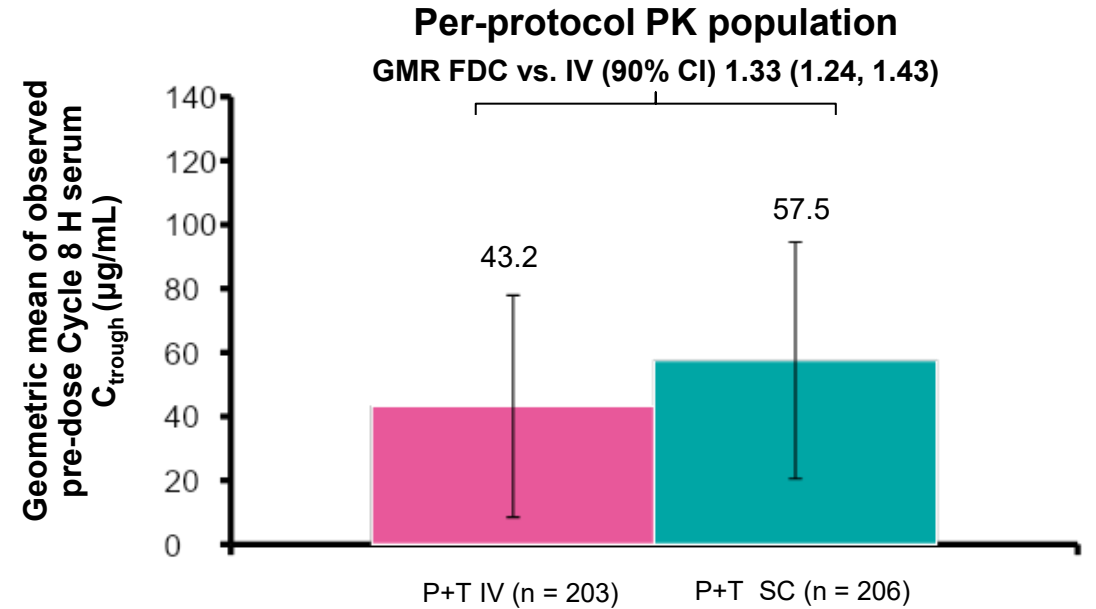
Primary endpoint: Non-inferiority of Cycle 7 (pre-dose Cycle 8) Pertuzumab serum C_{trough}
Key secondary endpoints: Non-inferiority of the Cycle 7 (pre-dose Cycle 8) Trastuzumab serum C_{trough} , tpCR, safety, IDFS, EFS, DRFI, OS

Fixed-dose combination of pertuzumab and trastuzumab for SC injection was **non-inferior** to pertuzumab + trastuzumab IV, based on Cycle 7 (pre-dose Cycle 8) pertuzumab and trastuzumab serum C_{trough} concentrations.

Primary endpoint: Pertuzumab serum C_{trough}

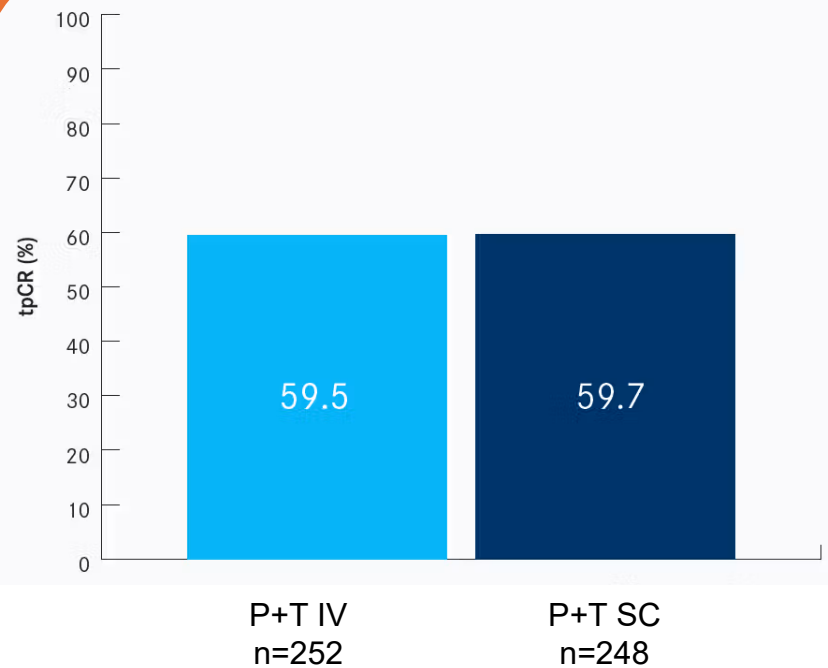


Secondary endpoint: Trastuzumab serum C_{trough}



473 patients [239 (95%) in the IV infusion group and 234 (95%) in the fixed-dose combination group] had a cycle 7 pharmacokinetic measurement (per-protocol PK population includes only patients who adhered to the pre-specified criteria for the schedule of PK assessments).

P+T SC had almost identical tpCR rates to P+T IV formulation



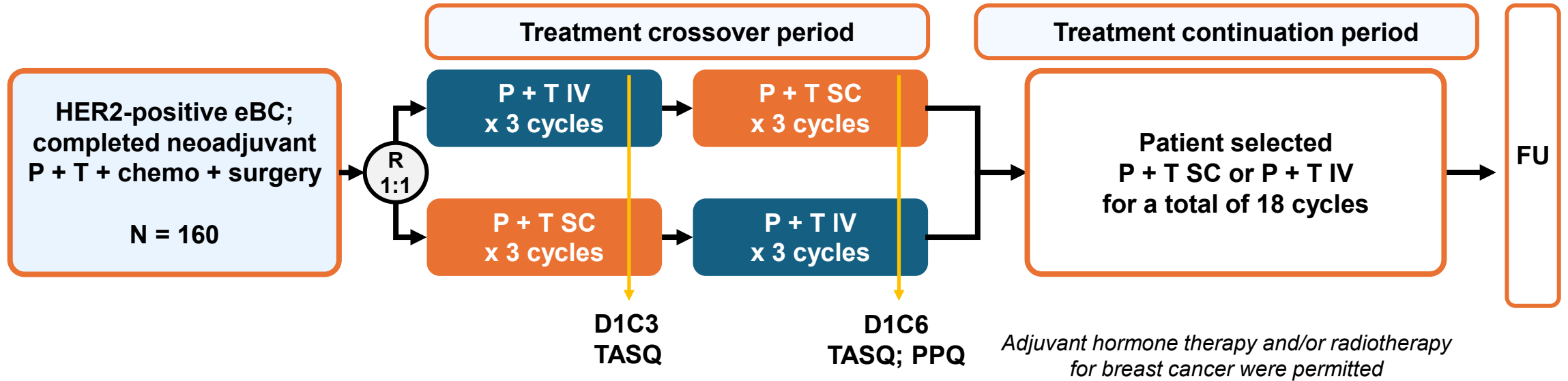
- Subgroup analyses generally consist with the main efficacy results. In particular, there was no discernible association between bodyweight and tpCR.
- tpCR rates are in keeping with data from previous studies of P+T IV + CT in neoadjuvant setting.

- The overall safety profile of the fixed-dose combination was similar to that intravenous infusions (including cardiac safety), with the exception of AEs related to the different routes of administration (ie, injection site reactions).
- The rates of treatment discontinuations due to AEs were similar between arms.
- Incidences of AEs were consistent with other studies that included pertuzumab + trastuzumab IV + chemotherapy

No. of patients, n (%)	P+T IV n = 252	P+T SC n = 248
Any AE	251 (99.6)	248 (100)
Grade ≥3 AEs	133 (52.8)	121 (48.8)
Serious AE	45 (17.9)	40 (16.1)
Death	1 (0.4)	1 (0.4)
Discontinued randomised anti-HER2 treatment due to AE	7 (2.8)	6 (2.4)

AEs (occurring in ≥30% of patients) ¹ No. of patients, n (%)	P+T IV n = 252	P+T SC n = 248
Alopecia	177 (70.2)	191 (77.0)
Nausea	152 (60.3)	146 (58.9)
Diarrhoea	139 (55.2)	145 (58.5)
Anaemia	103 (40.9)	84 (33.9)
Asthenia	76 (30.2)	70 (28.2)

PHranceSCa: study evaluating patient preference for P+T SC versus P+T IV



Stratification factors:

- Neoadjuvant chemotherapy regimen
- Neoadjuvant treatment response (pCR vs. non-pCR)
- Hormone receptor status

Primary objective: Patient preference for P+T SC

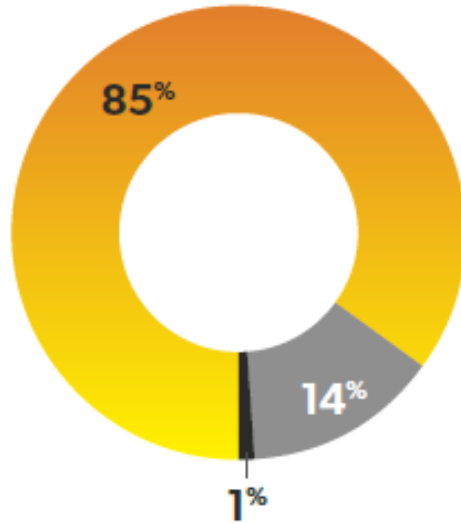
Key secondary objectives: Patient satisfaction; patients' choice of formulation for the continuation period; HRQoL, HCP perception of time/resource, safety and tolerability (including safety of switching from SC to IV formulations and vice versa), efficacy

PPQ= patient preference questionnaire

TASQ= therapy administration satisfaction questionnaire

Patient preference

“All things considered, which method of administration did you prefer?”



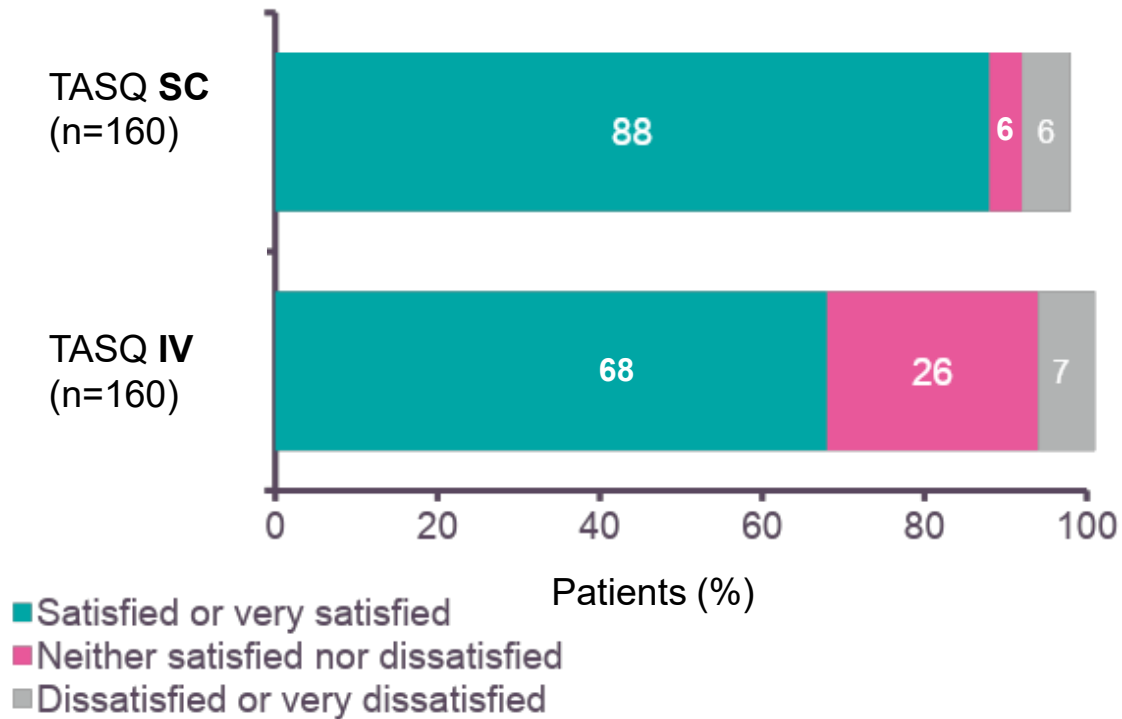
- Preferred P+T SC (n= 136/160)
- Preferred P+T IV (n= 22/160)
- No preference (n= 2/160)

No. patients, n (%)	P+T IV → P+T SC (n = 80)	P+T SC → P+T IV (n = 80)	All patients (N = 160)
Main reason for SC preference			
Total number of responses			
Requires less time in the clinic	143	139	282
Feels more comfortable during administration	60 (42.0) 41 (28.7)	59 (42.4) 32 (23.0)	119 (42.2) 73 (25.9)
Feels less emotionally distressing	21 (14.7)	25 (18.0)	46 (16.3)
Lower level of injection-site pain	14 (9.8)	18 (12.9)	32 (11.3)
Other reason	7 (4.9)	5 (3.6)	12 (4.3)

87% of patients chose to continue with P+T SC to complete their eBC treatment.

Patient-assessed therapy administration satisfaction

“How satisfied or dissatisfied were you with the SC injection or IV infusion?”



Treatment had no impact on patient–healthcare professional speaking time:

P+T SC: 85%

P+T IV: 79%

Most patients had more than enough time to talk to their healthcare professional during treatment:

P+T SC: 90%

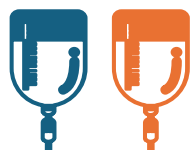
P+T IV: 83%

HCP (Healthcare professional) perception of time/resource

Drug preparation room

HCP estimate of total time in drug preparation room

P + H IV



15–20 mins

PH FDC SC

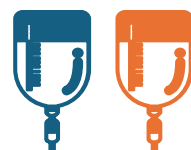


5 mins

Treatment room

HCP estimate of patient time in the treatment room

P + H IV



130–300 mins

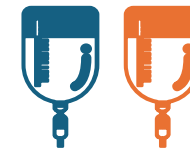
PH FDC SC



33–50 mins

HCP estimate of treatment administration time

P + H IV



60–150 mins

PH FDC SC



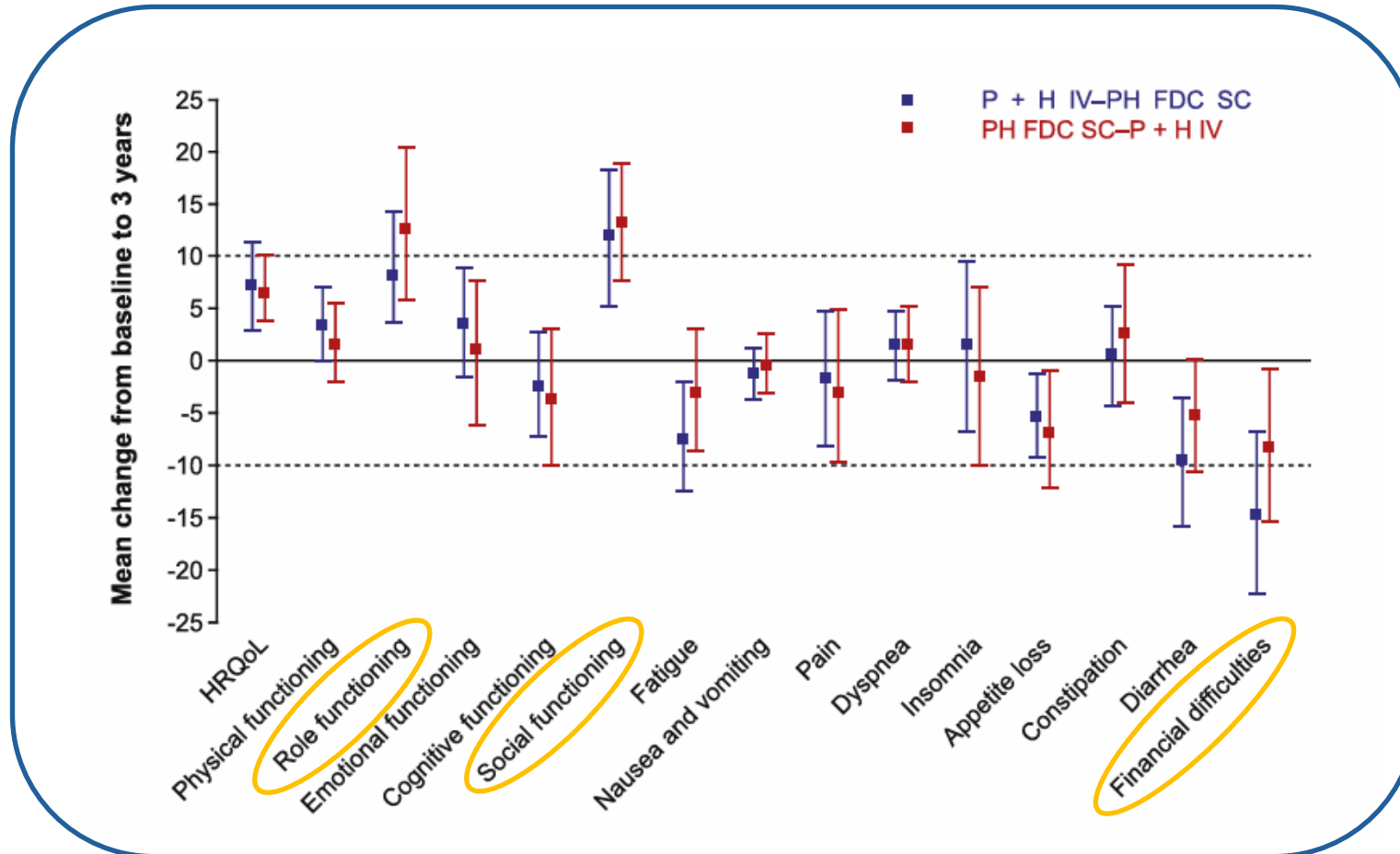
7–8 mins

- HCPs thought that **P+T SC** was the **quickest** from start of preparation to completion of administration for 88% of patients
- HCPs felt that **P+T SC** required **less resource usage** for preparation and administration, for 87% of patients
- HCPs agreed or strongly agreed that for 77% of patients, ready-to-use **P+T SC** resulted in **less drug wastage**

Safety: AE rates before and after switching were similar

	P +T IV → P+T SC		P+T SC → P+T IV		All patients (N = 160)
	P+T IV Cycles 1-3 (n = 80)	P+T SC Cycles 4-6 (n = 80)	P+T IV Cycles 1-3 (n = 80)	P+T SC Cycles 4-6 (n = 80)	
AEs	62 (77.5)	58 (72.5)	51 (63.8)	62 (77.5)	140 (87.5)
Five most common AEs (in ≥5% of patients), n (%)					
Radiation skin injury	17 (21.3)	7 (8.8)	10 (12.5)	10 (12.5)	43 (26.9)
Injection site reaction	0	12 (15.0)	0	24 (30.0)	36 (22.5)
Diarrhoea	12 (15.0)	7 (8.8)	4 (5.0)	6 (7.5)	25 (15.6)
Fatigue	5 (6.3)	4 (5.0)	4 (5.0)	5 (6.3)	15 (9.4)
Hot flush	6 (7.5)	4 (5.0)	0	5 (6.3)	15 (9.4)

✓ Long-term HRQoL



Mean changes from baseline were minimal, with no meaningful differences between arms.

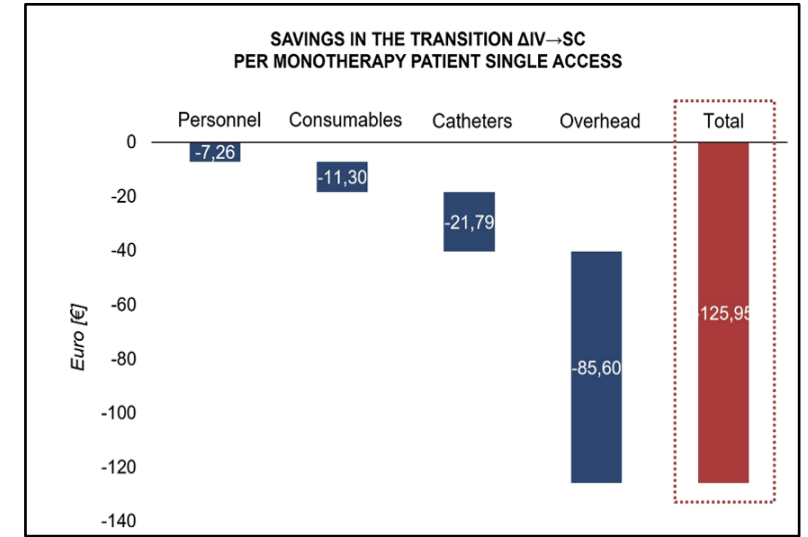
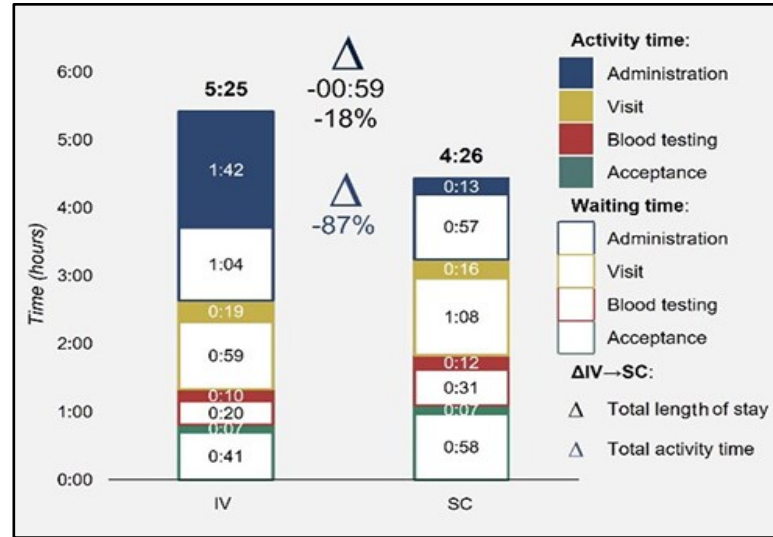
✓ Long-term Safety

Patients, n (%)	PH FDC SC Continuation (n = 138)	P + H IV Continuation (n = 21)
Any AE	92 (66.7)	14 (66.7)
Grade 3 AE*	7 (5.1)	2 (9.5)
Serious AE	4 (2.9)	0
Cardiac AE	1 (0.7)	1 (4.8)
Grade ≥ 3	0	0
Anaphylaxis/hypersensitivity	2 (1.4)	0
Grade ≥ 3	0	0
Administration-related reaction	16 (11.6)	1 (4.8)
Local injection-site reaction	13 (9.4)	0
Systemic injection reaction	2 (1.4)	0
Systemic infusion reaction	0	1 (4.8)
Grade ≥ 3 administration-related reaction	0	0
AE leading to dose interruption	8 (5.8)	1 (4.8)
AE leading to treatment discontinuation	0	1 (4.8)
AEs with incidence of ≥ 5% during the continuation period (any grade)		
Diarrhea	15 (10.9)	4 (19.0)
Injection-site reaction	13 (9.4)	0
Arthralgia	6 (4.3)	3 (14.3)
Fatigue	7 (5.1)	1 (4.8)
Pruritus	7 (5.1)	0
Pain in extremity	4 (2.9)	2 (9.5)
Rash	2 (1.4)	3 (14.3)
Headache	1 (0.7)	2 (9.5)
Myalgia	1 (0.7)	2 (9.5)
Bone pain	0	2 (9.5)

PHASTER study: economic and organizational impact of SC P+T combination

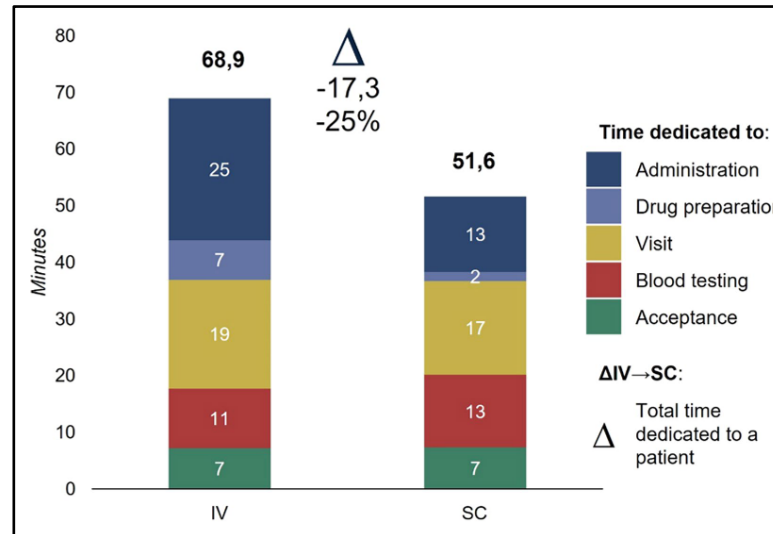
Patients' pathway time:

Reduction in the length of stay within the DH, driven by the administration phase.



Personnel time:

Considering all the phases, the SC formulation takes 17 min less than IV for the health care professionals (specifically to the pharmacist and the nurse) involved in the patient pathway.



Direct cost for the Hospital

The use of SC formulation reduces direct costs for the hospital.



Indications

Early Breast Cancer

PHESGO® (pertuzumab, trastuzumab, and hyaluronidase-zzxf) is indicated for use in combination with chemotherapy for

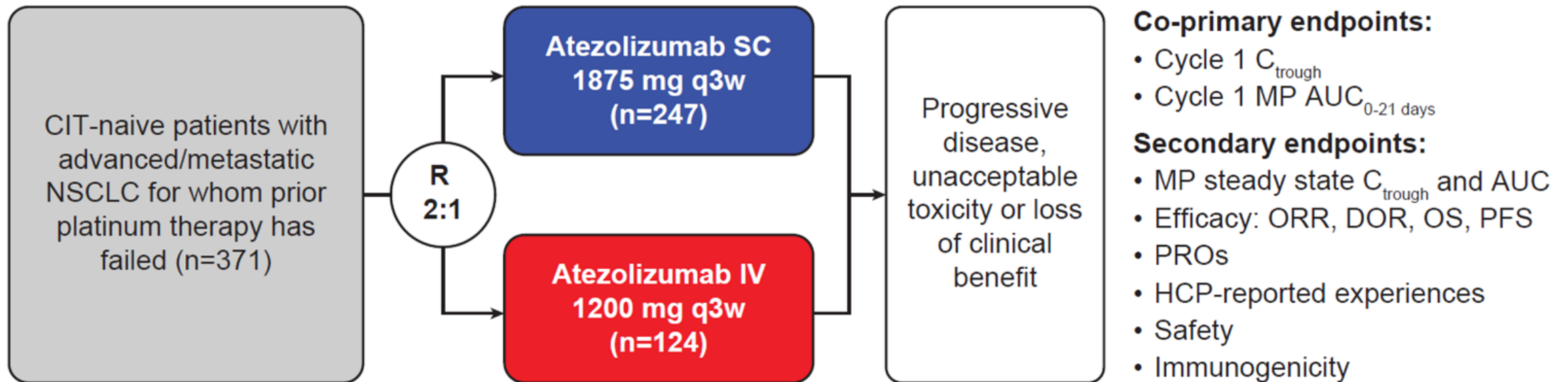
- the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node-positive) as part of a complete treatment regimen for early breast cancer (EBC)
- the adjuvant treatment of adult patients with HER2-positive EBC at high risk of recurrence

Metastatic Breast Cancer

PHESGO is indicated for use in combination with docetaxel for the treatment of adult patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

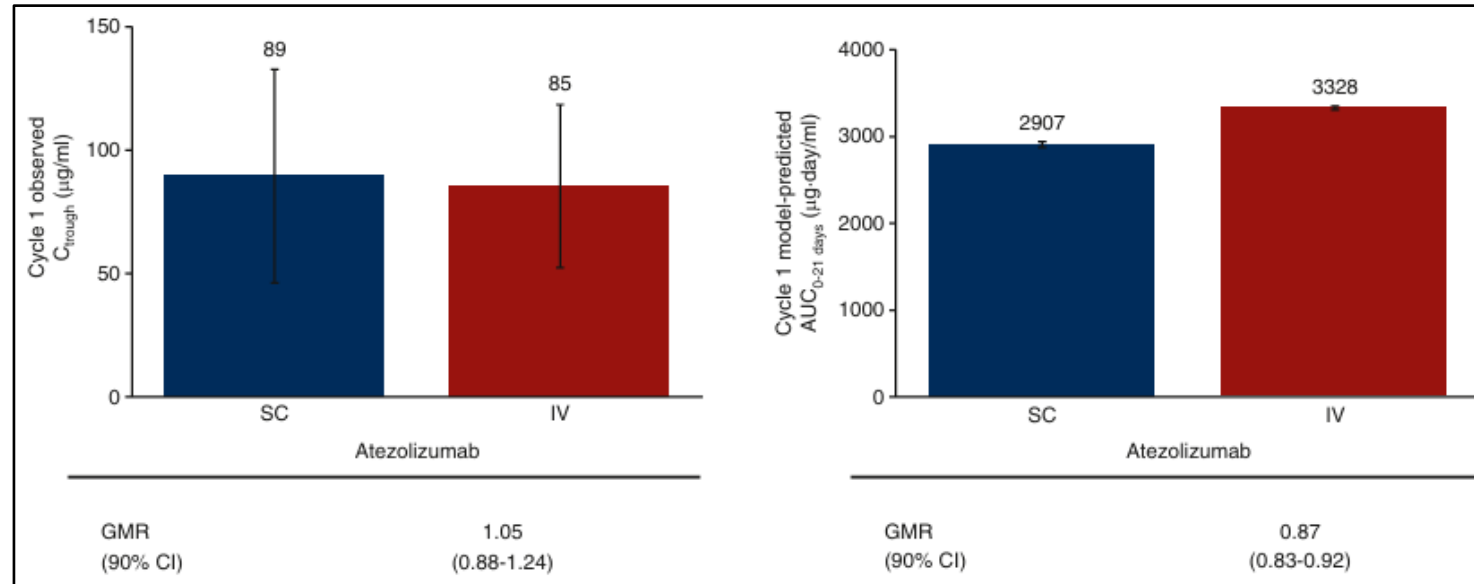
SC Atezolizumab formulation in TN MBC

IMscin001 (Part 2) trial:

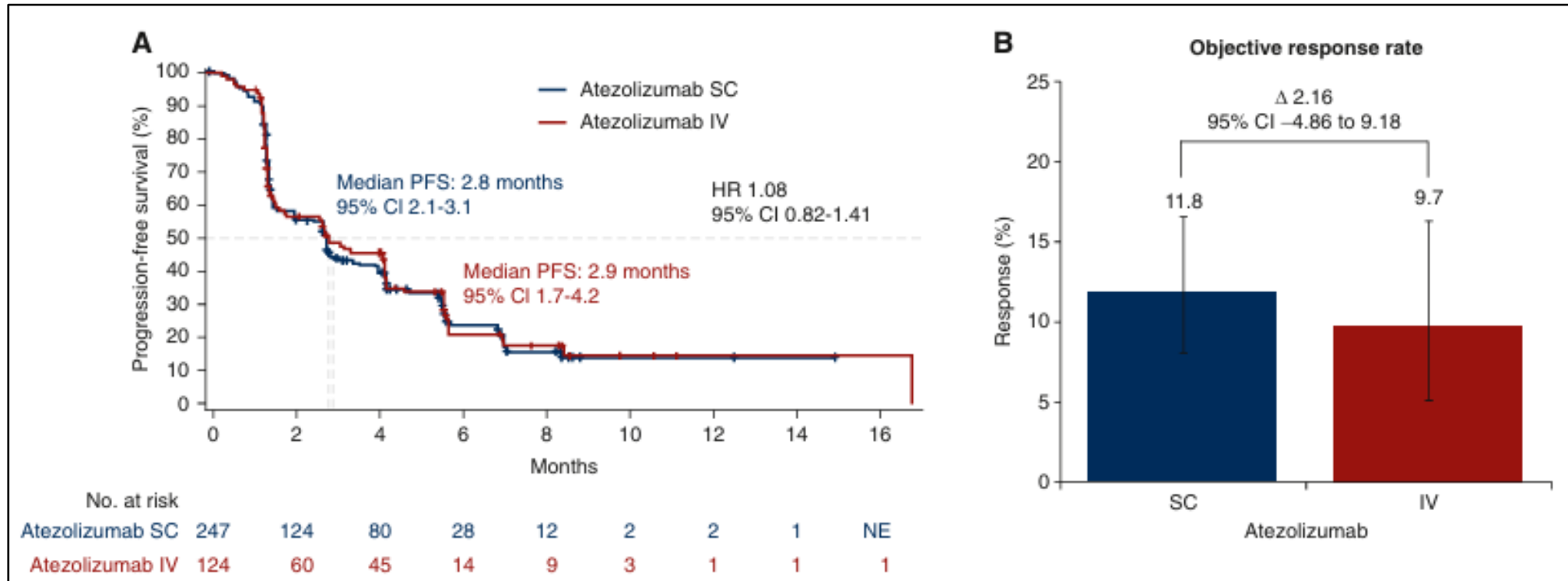


Exposure of atezolizumab SC was non-inferior to IV

Geometric Mean (% Coefficient of Variation)		Atezolizumab		
		SC	IV	GMR (90% CI)
Co-primary endpoints	Cycle 1 Observed^a C_{trough} μg/mL	89.4 (43.2)	85.4 (33.0)	1.05 (0.88 , 1.24)
	MP^b Cycle 1 AUC_(0-21d) μg·d/mL	2907 (32.2)	3328 (20.2)	0.87 (0.83 , 0.92)
Secondary endpoints	MP^b C_{trough} at steady state μg/mL	205 (45.9)	179 (35.6)	
	MP^b AUC at steady state μg·d/mL	6163 (39.6)	6107 (26.4)	



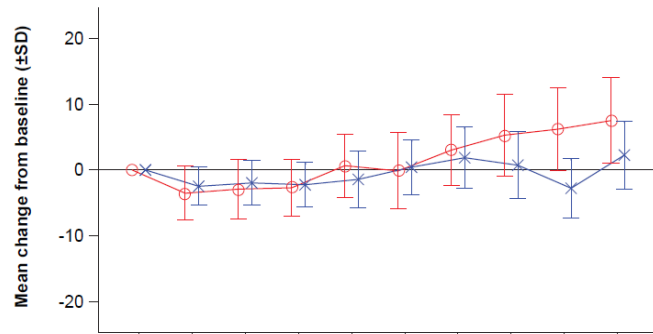
Efficacy was similar between arms



Patient-reported outcomes

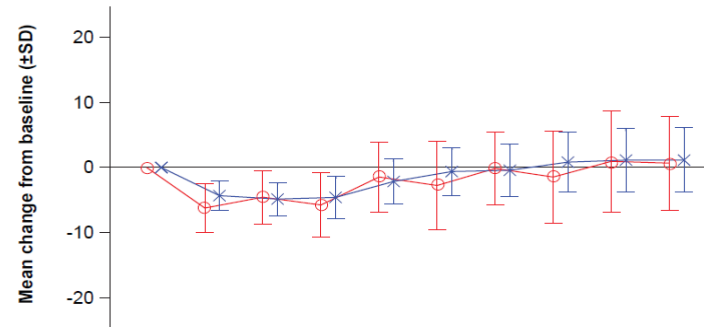
- Completion rates for PROs remained above 90% through Cycle 14
- Mean change from baseline scores were similar over time, with largely overlapping 95% CIs for global health status, physical functioning and role functioning through the Cycle 14 timepoint

Global health status



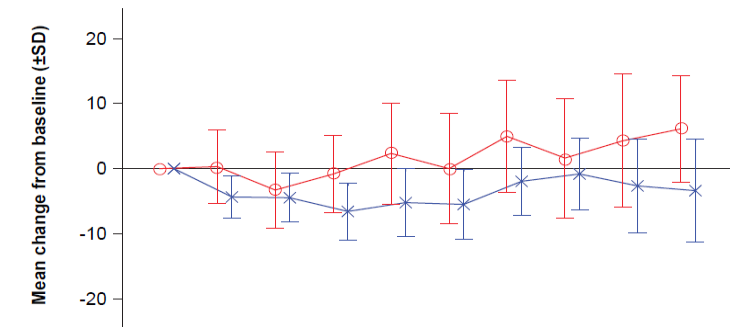
No. contributing data	BL	C2	C3	C4	C5	C6	C8	C10	C12	C14
SC	242	218	182	167	134	118	94	81	69	59
IV	117	106	86	80	64	58	47	41	35	30

Physical functioning



No. contributing data	BL	C2	C3	C4	C5	C6	C8	C10	C12	C14
SC	243	219	183	167	134	119	95	81	70	59
IV	117	106	86	80	64	58	47	41	35	30

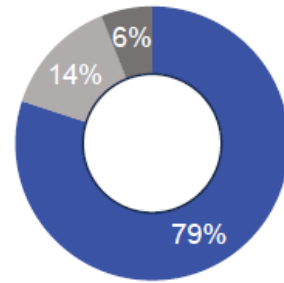
Role functioning



No. contributing data	BL	C2	C3	C4	C5	C6	C8	C10	C12	C14
SC	242	218	182	167	134	118	94	81	69	59
IV	117	106	86	80	64	58	47	41	35	30

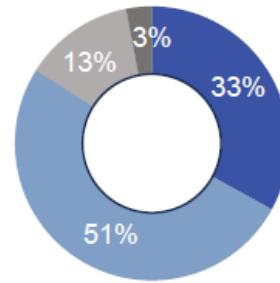
HCP-reported experiences

Do you think atezolizumab SC is convenient?



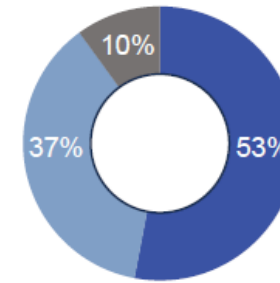
■ Yes
■ Unsure
■ No

Overall, how satisfied were you with atezolizumab SC?



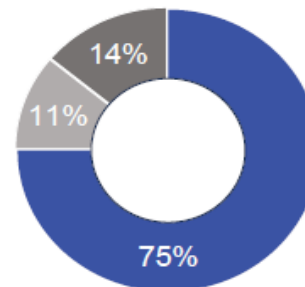
■ Very satisfied
■ Satisfied
■ Dissatisfied
■ Very dissatisfied

Overall, how easy did you find atezolizumab administration?



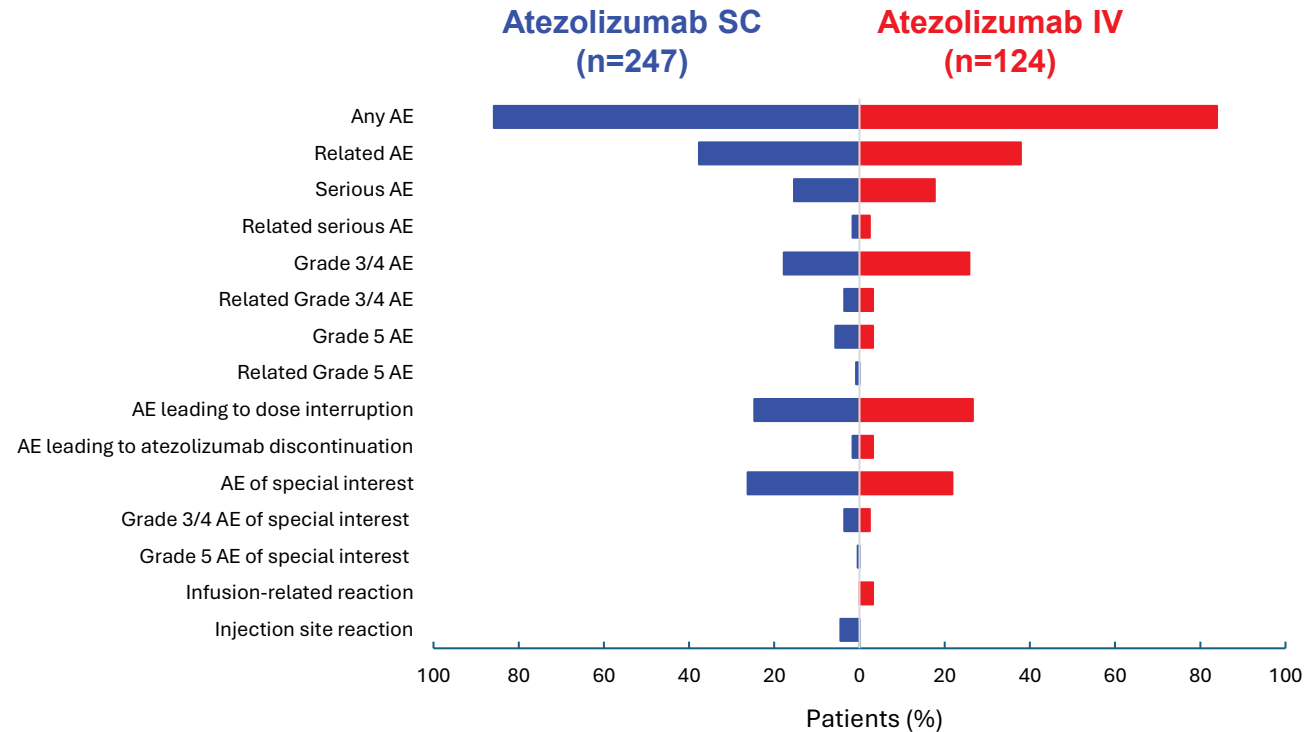
■ Very easy
■ Fairly easy
■ Not at all easy

If used in routine practice, do you think administering atezolizumab SC could save staff time compared with atezolizumab IV?



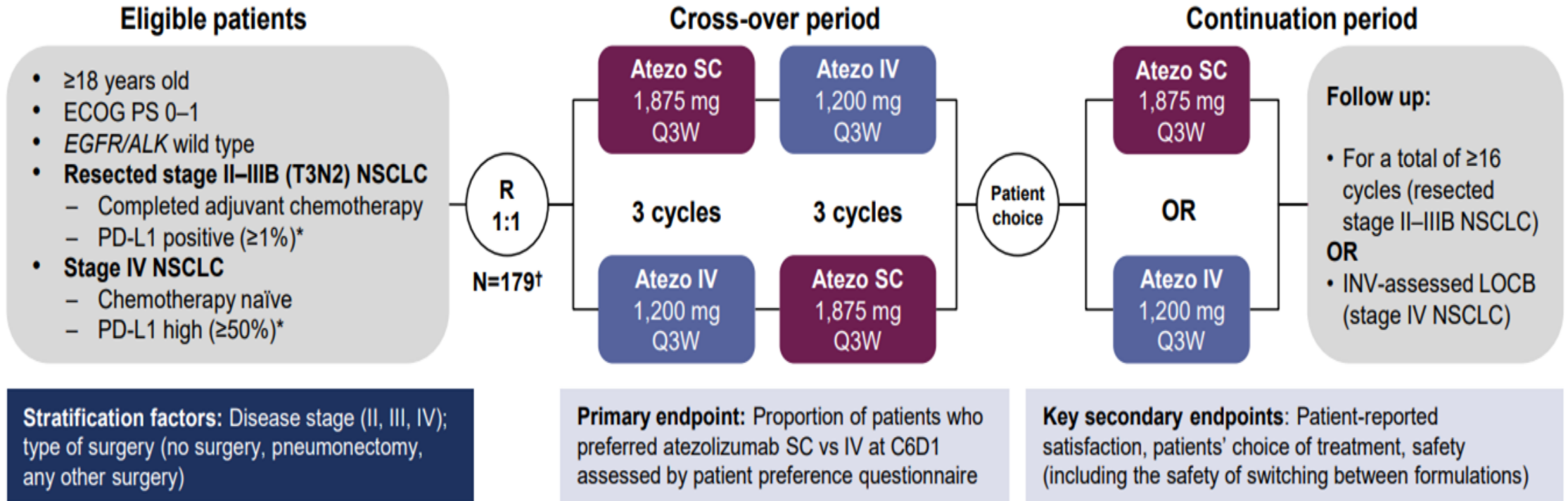
■ Yes
■ Unsure
■ No

Safety



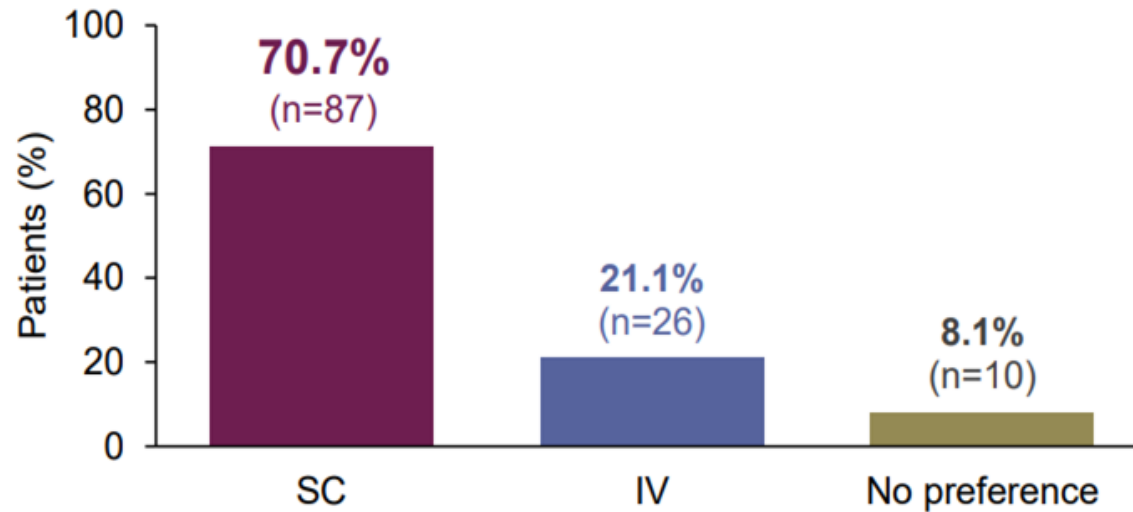
- No new safety signals were identified
- Infusion-related reactions occurred in 3.2% of patients in the IV arm and no patients in the SC arm
- Number of injection site reactions was low and mild in nature (mostly Grade 1)

IMscin002 trial:



Patient-reported outcomes

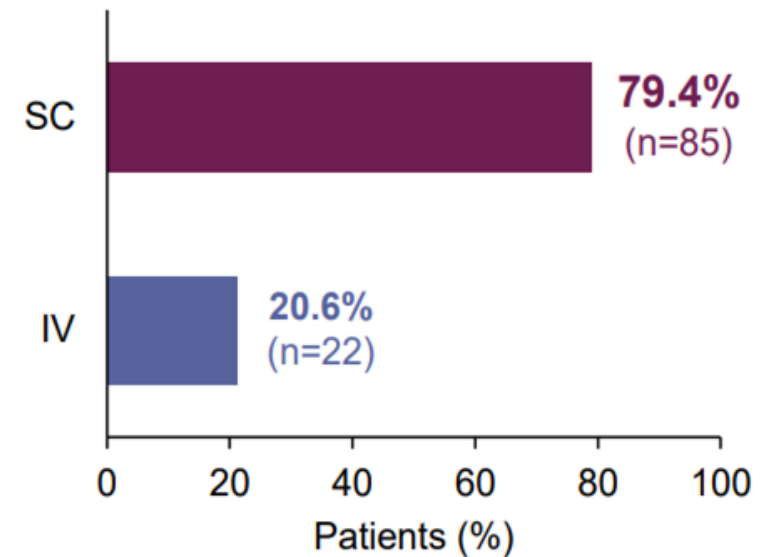
Primary endpoint: Patients' preferred administration method (assessed by questionnaire†) (n=123)



Patient's main reasons for preferring **atezolizumab SC**:

- Requires **less time the clinic** (64.4%, n=56)
- Feels **more comfortable** (46.0%, n=40)
- Is **less emotionally distressing** (29.9%, n=26)

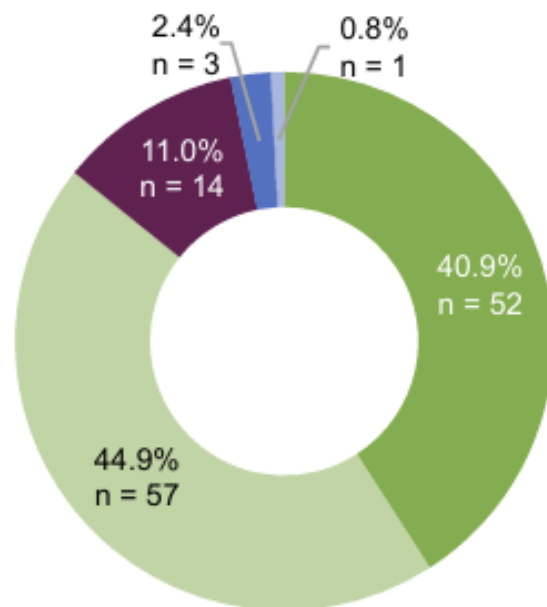
Secondary endpoint: Patients' choice of treatment for the continuation period (n=107)



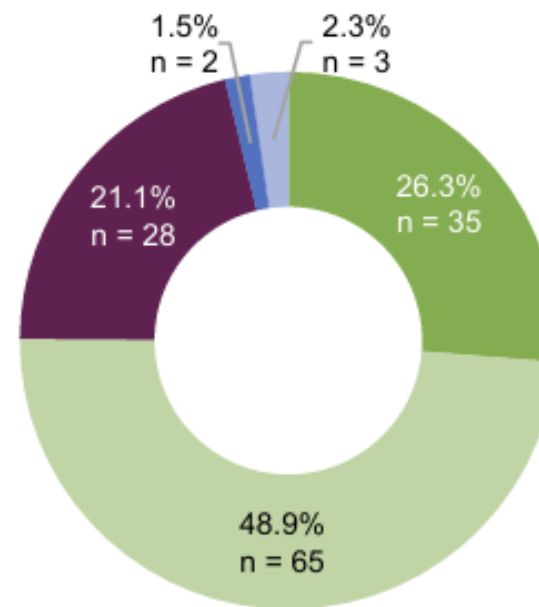
All patients who preferred **atezolizumab SC** chose **SC** for the continuation period

Patient-reported satisfaction

Patient satisfaction with atezolizumab SC (n = 127)*



Patient satisfaction with atezolizumab IV (n = 133)†



Very satisfied Satisfied Neither satisfied nor dissatisfied Dissatisfied Very dissatisfied

Overall, **85.8%** of patients were very satisfied/satisfied with **atezolizumab SC** vs **75.2%** of patients with **IV**

Safety

- The overall safety profile (cross over and continuation)* was consistent with the **established atezolizumab safety profile**¹⁻³
 - **No new safety concerns** were identified
- **Switching between atezolizumab SC and IV**, regardless of sequence, was **well tolerated**
 - The likelihood of a patient experiencing an injection-site reaction or infusion-related reaction event did not increase when switching between **atezolizumab SC** and **IV**, or vice versa

Patients, n (%)	Cross-over Atezolizumab SC / IV		Cross-over Atezolizumab IV / SC		All patients
	C1–C3 (n=86)	C4–C6 (n=71)	C1–C3 (n=89)	C4–C6 (n=69)	C1–C6 (n=175)
≥1 AE	47 (54.7)	38 (53.5)	56 (62.9)	27 (39.1)	121 (69.1)
Related AE	31 (36.0)	22 (31.0)	28 (31.5)	21 (30.4)	81 (46.3)
AE with fatal outcome	3 (3.5)	0	1 (1.1)	1 (1.4)	5 (2.9)
Related AE with fatal outcome	1 (1.2)	0	0	0	1 (0.6)
Serious AE	11 (12.8)	4 (5.6)	11 (12.4)	2 (2.9)	28 (16.0)
Related serious AE	4 (4.7)	2 (2.8)	4 (4.5)	2 (2.9)	12 (6.9)
Highest Grade 3–4 AE	13 (15.1)	7 (9.9)	15 (16.9)	0	34 (19.4)
Related highest Grade 3–4 AE	5 (5.8)	1 (1.4)	6 (6.7)	0	12 (6.9)
AE leading to treatment discontinuation	5 (5.8)	2 (2.8)	7 (7.9)	2 (2.9)	16 (9.1)
AE leading to treatment interruption	9 (10.5)	7 (9.9)	7 (7.9)	2 (2.9)	24 (13.7)



«Tecentriq» in associazione con nab-paclitaxel e' indicato per il trattamento di pazienti adulti con carcinoma mammario triplo negativo (triple-negative breast cancer, TNBC) non resecabile localmente avanzato o metastatico, i cui tumori presentano un'espressione di PD-L1 $\geq 1\%$ e che non sono stati sottoposti a precedente chemioterapia per malattia metastatica.

Conclusions



There is a trend to move care for patients with breast cancer outside hospitals, especially where the evidence of benefit has been established

SC formulations are quicker to administer and more convenient for patients, carers and HCPs versus IV formulations

Fixed-dose formulations help reduce dosing errors and simplify drug preparation and administration

SC formulations have shown no new safety signals versus IV formulations and were generally well tolerated

Thanks for attention!



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