

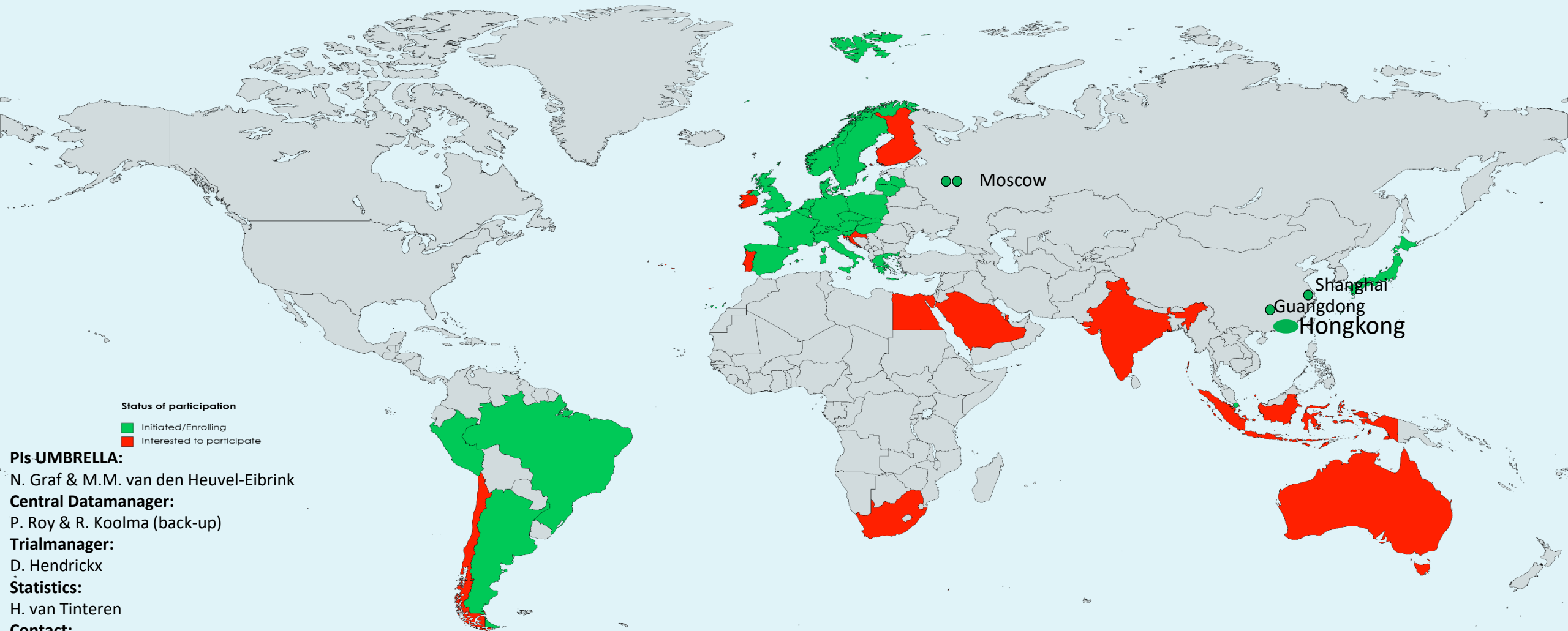


# UMBRELLA PROTOCOL

## SIOP-RTSG 2016



Newsflash #57  
June 2024



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# UMBRELLA: newsflash June 2024 Participating (as of the 31<sup>th</sup> of May 2024)

#	Countries	Upload names in SIOP-RTSG website	Ethical approval	NCC contract with sponsor	Initiation date	First patient Registered
1	Germany	x	x	x	22-03-2019	29-07-2021
2	Netherlands	x	x	x	22-03-2019	07-06-2019
3	Italy	x	x	x	12-04-2019	20-06-2019
4	Spain	x	x	x	07-06-2019	03-07-2019
5	Greece	x	x	x	13-06-2019	10-07-2019
6	Brazil	x	x	x	24-06-2019	11-07-2019
7	France	x	x	x	22-07-2019	23-10-2019
8	Shanghai (Regional site)	x	x	x	22-07-2019	25-09-2019
9	UK	x	x	x	04-09-2019	21-10-2019
10	Norway	x	x	x	16-12-2019	10-02-2020
11	Denmark	x	x	x	16-12-2019	12-06-2020
12	Switzerland	x	x	x	28-02-2020	08-05-2020
13	Guangdong, (Regional site), China	x	x	x	20-05-2020	29-06-2020
14	Moscow-DRO, (Regional site), Russia	x	x	x	29-05-2020	30-06-2020
15	Belgium	x	x	x	19-06-2020	24-09-2020
16	Hungary	x	x	x	07-08-2020	31-08-2020
17	Moscow-NBO, (Regional site), Russia	x	x	x	28-09-2020	20-11-2020
18	Singapore	x	x	x	30-11-2020	11-01-2021
19	Poland	x	x	x	22-1-2021	8-4-2021
20	Austria	X	X	X	7-6-2021	16-7-2021



## UMBRELLA: newsflash June 2024 Participating (as of the 31<sup>th</sup> of May 2024)

#	Countries	Upload names in SIOP-RTSG website	Ethical approval	NCC contract with sponsor	Initiation date	First patient Registered
21	Czech Republic	X	X	X	23-7-2021	30-03-2022
22	Sweden	X	X	X	14-3-2022	29-11-2023
23	Slovenia	X	X	X	08-4-2022	09-08-2022
24	Argentina	x	x	x	29-04-2022	12-05-2022
25	Peru	x	x	x	18-10-2022	
26	Slovakia	x	X	x	28-10-2022	23-05-2023
27	Japan	X	x	x	25-01-2023	27-03-2023
28	Latvia	x	x	x	10-03-2023	28-03-2023
29	Hong Kong	x	x	x	14-04-2023	07-12-2023
30	Lithuania	x	x	x	21-04-2023	

# UMBRELLA: newsflash June 2024 Preparing initiation

(as of the 31<sup>th</sup> of May 2024)



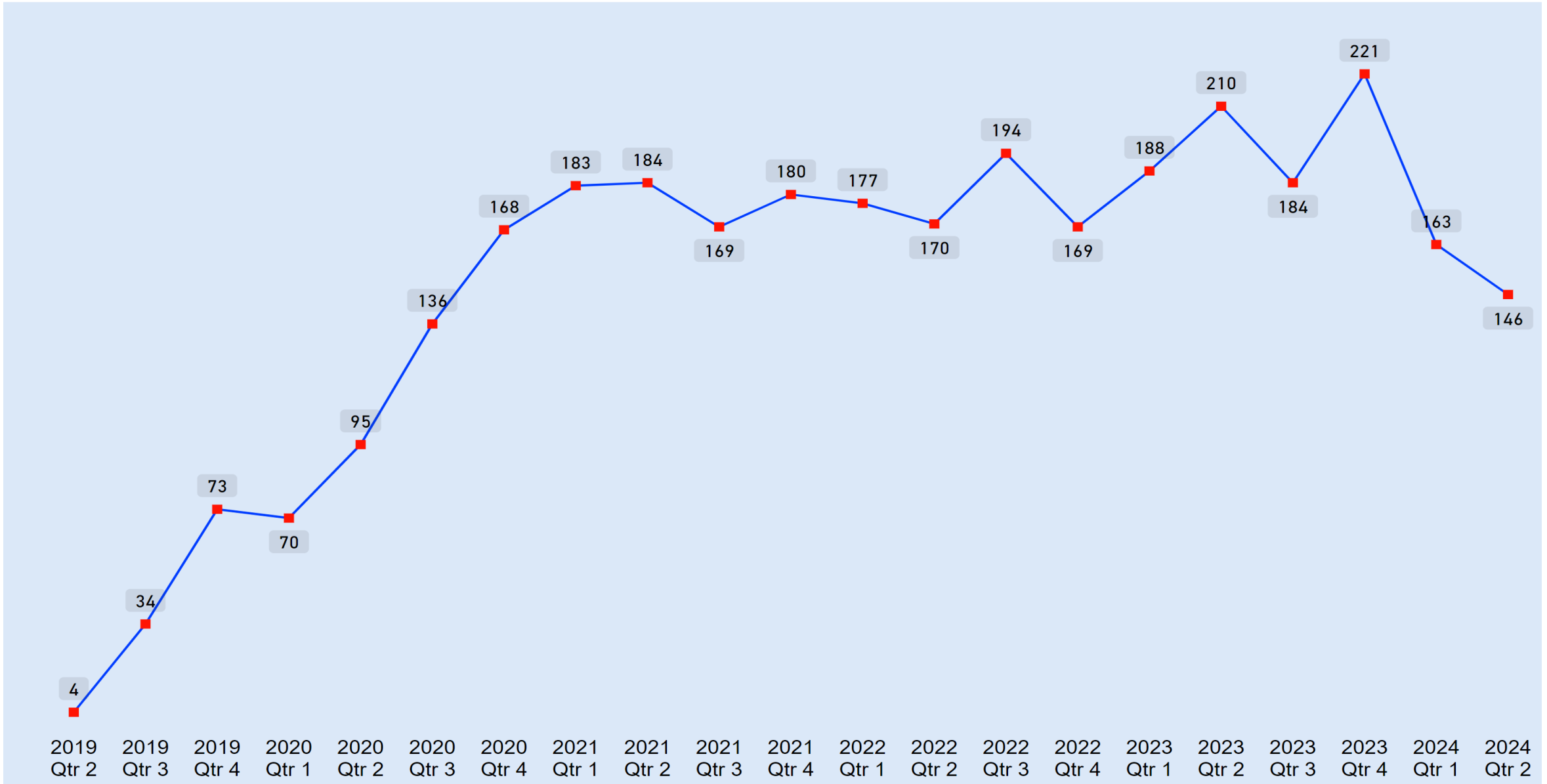
	Countries	Upload names in SIOP-RTSG website	Ethical approval	NCC contract with sponsor	Initiation visit by the SIOP RTSG office
27	Chile				
28	Croatia	Completed	Completed		
29	Egypt	Pending	Pending	Pending	
30	Finland				
31	Indonesia				
32	Ireland	Completed	Pending	Pending	
33	Portugal				
34	Qatar	Completed			
35	South Africa				
36	Kazachstan				
37	Saudi Arabia	Completed	Completed	Completed	CIV can be scheduled
38	India				

\*) CIV is Country initiating visit

# UMBRELLA: total enrolment per month

(as of the 31<sup>th</sup> of May 2024)

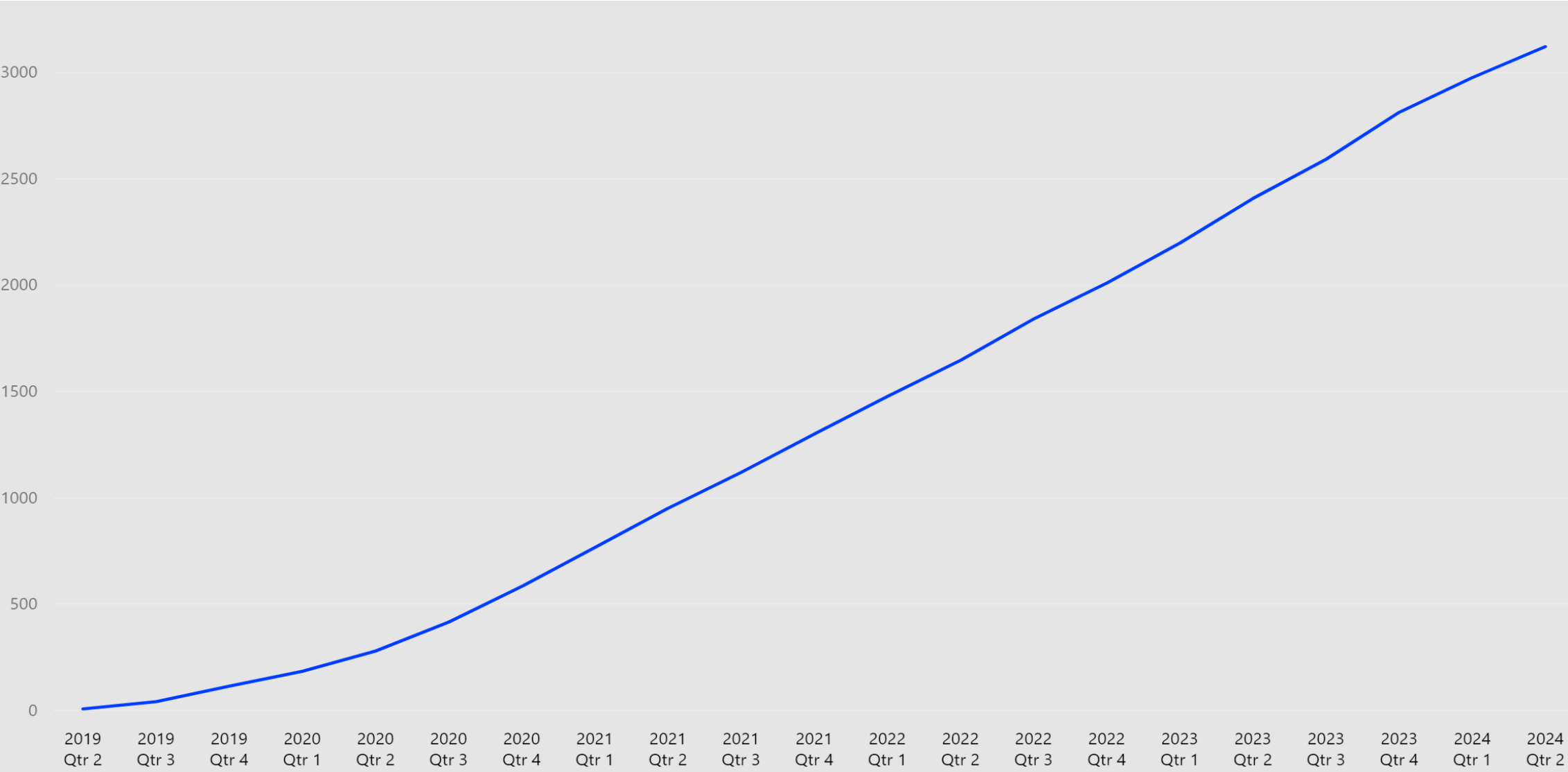
Total enrolment = 3342



# UMBRELLA: cumulative incidence

(as of the 31<sup>th</sup> of May 2024)

Total enrollment = 3342

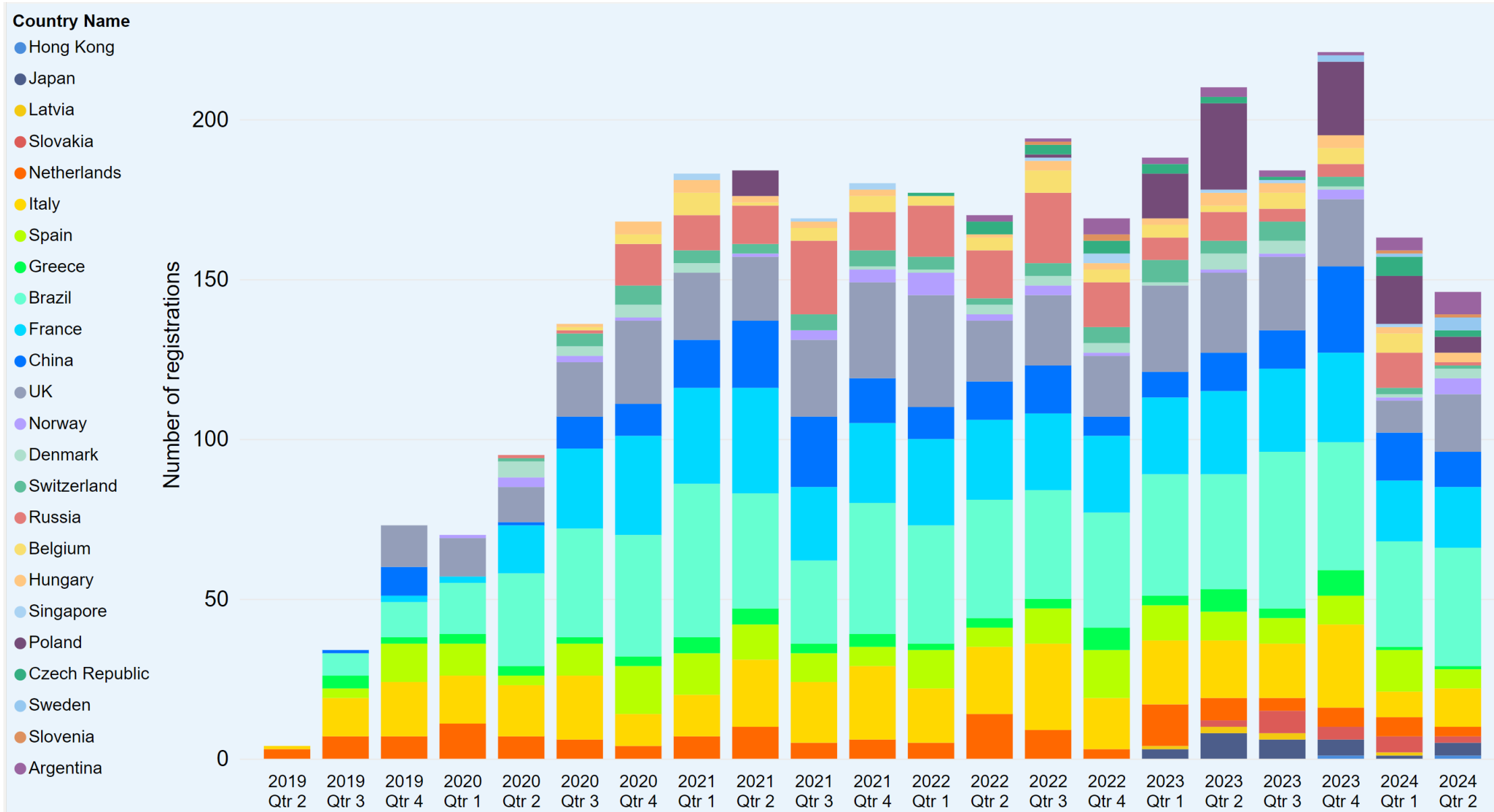


# UMBRELLA: country specific enrolment

(as of the 31<sup>th</sup> of May 2024)



Total enrolment= 3342



# UMBRELLA: monthly enrolment as per recruiting national/regional sites

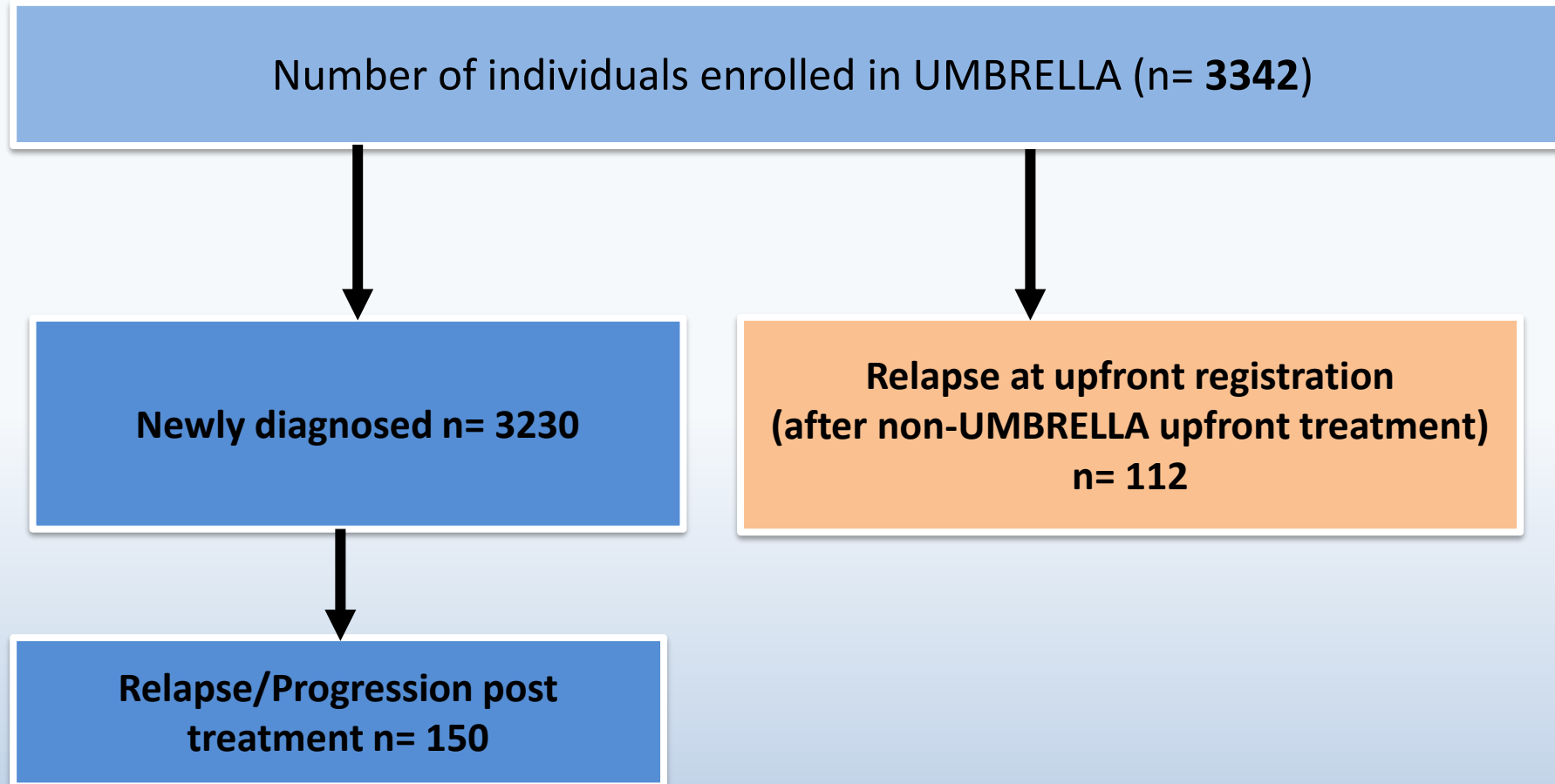
(as of the 31<sup>th</sup> of May 2024)



	Arge ntin a	Au stri a	Belg ium	Brazil	Czech Republic	Den mark	France	Greece	Germa ny	Hong Kong	Hungary	Italy	Japan	Latvia	Nethe rland s	Norway	Poland	Singa pore	Slova kia	Slove nia	Spain	Sweden	Switzer land	UK	China- 01	China- 02	Russ ia-01	Russi a-02	Grand Total
<b>2019 Total</b>				18			2	6				30			17						15		13	10					111
<b>2020 Total</b>			4	117		12	73	11			5	61			28	7					38		11	66	7	14	5	10	469
<b>2021 Total</b>		2	17	151		4	111	17	4		10	76			28	8	8	5			39		17	95	26	46	29	29	722
<b>2022 Total</b>	8	0	18	144	12	10	100	15	77		6	81			31	13	1	4		3	44		15	95	8	35	30	37	787
Jan	1	0	1	10	2	0	7	1	4		0	6			3	0	1	0		0	5		3	7	0	1	3	2	57
Feb	0	0	2	13	0	1	8	1	6		0	7			4	0	0	0		0	3		1	11	0	3	0	2	62
March	1	0	1	15	1	0	9	1	8		2	7	3	1	6	0	13	0		0	3		3	9	0	4	0	0	87
April	2	0	0	12	1	2	6	0	16		0	6	0	1	2	1	12	1		0	2		1	4	0	5	5	3	82
May	0	0	0	13	0	0	6	5	6		1	7	1	1	3	0	15	0	1	0	4		0	9	0	3	0	0	75
June	1	0	2	11	1	3	14	2	8		3	5	7	0	2	0	0	0	1	0	3		3	12	0	4	1	0	83
July	1	0	1	18	1	2	8	2	8		2	6	6	0	2	1	0	1	2	0	3		0	6	6	1	1	0	77
Aug	1	1	1	15	0	2	8	1	12		0	6	0	0	0	0	0	0	4	0	2		3	6	0	3	2	0	68
Sep	0	0	3	16	0	1	12	0	8		1	5	0	2	2	0	0	0	1	0	3		3	11	0	2	1	0	68
Oct	0	0	2	10	0	0	16	6	6		2	12	0	0	1	3	0	0	0	0	1		1	11	0	2	0	0	73
Nov	0	0	0	14	0	1	6	2	6		2	6	0	0	5	0	0	0	2	0	2	1	1	8	0	4	0	0	61
Dec	1	0	3	16	0	0	6	0	11	1	0	8	5	0	0	0	23	0	2	0	6	1	1	2	15	6	4	0	111
<b>2023 Total</b>	8	1	16	163	6	11	104	21	100	1	13	81	22	5	30	5	64	2	13	0	37	2	20	96	21	38	17	7	904
Jan- 2024	2	1	3	9	4	0	4	0	7	0	1	2	1	0	1	0	6	0	2	1	6	0	0	5	2	3	0	0	60
Feb- 2024	0	0	3	7	2	1	11	0	7	0	1	1	0	1	4	1	0	1	1	0	3	0	2	3	2	0	2	9	63
Mar- 2024	2	1	0	17	0	0	4	1	4	0	0	5	0	0	1	0	9	0	2	0	4	1	0	2	4	4	0	0	61
Apr- 2024	5	0	0	20	2	0	8	1	13	0	1	5	4	0	1	3	2	0	1	0	4	2	0	11	2	3	1	0	89
May- 2024	2	3	0	17	0	3	11	0	4	1	2	7	0	0	2	2	3	0	1	1	2	2	1	7	3	3	0	0	77
<b>Grand Total</b>	27	8	61	663	26	41	428	72	216	2	39	349	27	6	143	39	93	12	20	5	192	7	66	393	85	146	84	92	3342

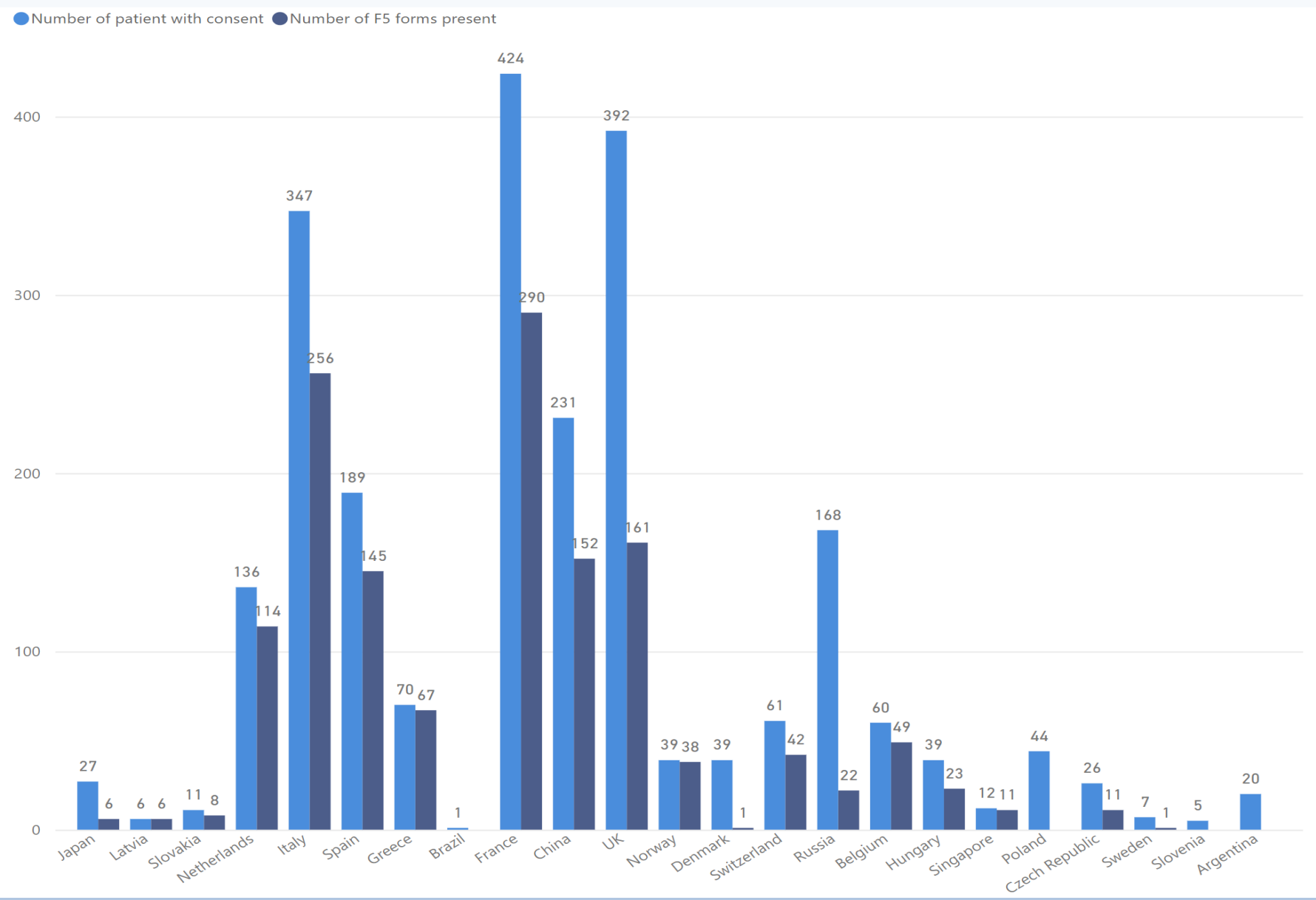


# Enrollment UMBRELLA



Of the patients with completed national reference pathology review(F15), n=1830 , n=448 were non-WT (24.5%)

# Biobanking Informed consent(F0)(total no =2354) vs F5 (total no= 1403) available



Please register your biobanked material through form F5!!!!

# SIOP-RTSG-UMBRELLA: what's new?



## Inclusion summary:

- 30 National/Regional Coordinating Centres are now initiated, 28 enrolling now
- Total enrollment: **3342** unique patients(including relapsed patients from alternative studies, and non-WT)

## Please remember:

- Filling in all registration, end-of treatment and follow-up forms during and after therapy is urgently requested!!!!!!
- Please pay special attention to completing Forms F5, F6, F7, for all patients (Biobanking, radiotherapy and postoperative chemo)
- We had all NCs regarding the retrieval on missing clinical, tumor and molecular data. Please fill in your missing data of all registered patients ASAP, an excell file template will be send soon for the 1 qgain data and other included biomarkers

# UMBRELLA: Recurrent addendum (I)



## Logistics before initiation of a country

### National coordinator :

- Completion of registration of the full team on the intranet (template <http://siop-rtsg.org>).
- Ethical approval
- Sponsorship contract (with Homburg)

### Thereafter,

- Send these documents to the SIOP-RTSG office([SIOP-Umbrella-DM@prinsesmaximacentrum.nl](mailto:SIOP-Umbrella-DM@prinsesmaximacentrum.nl))
- The SIOP RTSG-office will plan an initiation visit (by Zoom)
- All personnel that will enter data, gets access to the ALEA database by the SIOP-RTSG office (after database training)

In case of any questions at any time, please contact the SIOP-office([SIOP-Umbrella-DM@prinsesmaximacentrum.nl](mailto:SIOP-Umbrella-DM@prinsesmaximacentrum.nl))

### Initiation of local sites:

- After initiation of a country/region, initiation of local sites is the responsibility of the national/regional coordinator

# UMBRELLA: Recurrent addendum (II)

## Ongoing biological and add-on studies



- Please **biobank** on a national level **and** fill in the biobanking form (F5). (Otherwise your biobanked samples are not visible)
- Please complete every form in the database (SAVE) but also **SUBMIT** each form.
- Please register also all **non-WT** cases, adult WT and relapses
- **The Randomet trial (for stage IV) is open!** (Stage IV, RCT), PIs: A Verschuur and R Furtwangler (separate reporting)
- The **miRNA study** by Eckart Meese is launched
- Please (encourage all your co-workers to) become members of SIOF-RTSG. The application form can be found on the <http://siop-rtsg.org> website.
- Protocol amendment 3.2 dd MAY2022 was approved by the German EC. The protocol and approval can be found on the website. Please submit this to your EC as soon as possible, and change and **(before submission) the Patient information sheet TO OBTAIN INFORMED CONSENT to draw 4 extra blood samples (4 time points) for liquid biopsy research, after discontinuation of treatment, before you submit the amendment(see biology chapter)**

## Addendum III. The amendment of the UMBRELLA protocol is approved by the ethical committee in Germany of the sponsor.

The amended and approved version (May 2022) is placed (in October 2022) on the SIOP-RTSG website in the intranet environment (<http://siop-rtsg.org> under protocols), be aware that:

- The amended protocol is split in 2 parts, A and B
- The approval letter can be found under ethical approval
- For European countries: it is advised to submit the amendment as soon as possible to your ethical committees. Although the newly introduced European Clinical Trial Regulation (ECTR) allows for submittance of amendments of protocols approved under the Clinical Trial Directive, it is uncertain whether there will be any "obstructive" issues

### Summary of content of the Amendments of the SIOPRTSG -2016- UMBRELLA protocol:

- Harmonization of chemotherapy adjustments advise during and after RT, through-out the protocol (avoid dox and ActD 1 week before, until 2 weeks after the end of RT)
- Dose adjustments of infants (including for irinotecan) is harmonized, through-out the whole protocol document
- A recommendation for functional asplenia after RT is added (based on the paper of Arunagiri, EJC, 2021)
- In Stage IV, local stage III, totally necrotic WTs, abdominal RT is advised to be omitted (based on R Fajardo Davilla, Cancers 2021)
- Guideline for fertility counselling and preservation is added (based on 3x (female, male and ethics) Lancet Oncology, Mulders et al, 2021)
- For surveillance of kidney function urine dipstick (unreliable) is replaced by urine proteinuria assessment
- Biobanking section now includes recommendations for viable biospecimen processing and storage
- Treatment recommendations for nephroblastomatosis and predisposition, are listed in stage V, but also in the localized WT stage section
- Biopsy recommendations are refined (based on the T Jackson paper, PBC, 2022)
- The paragraph on IDMC regulations is omitted (is not applicable)
- 4 extra biosamples for liquid biospies after discontinuation of therapy