

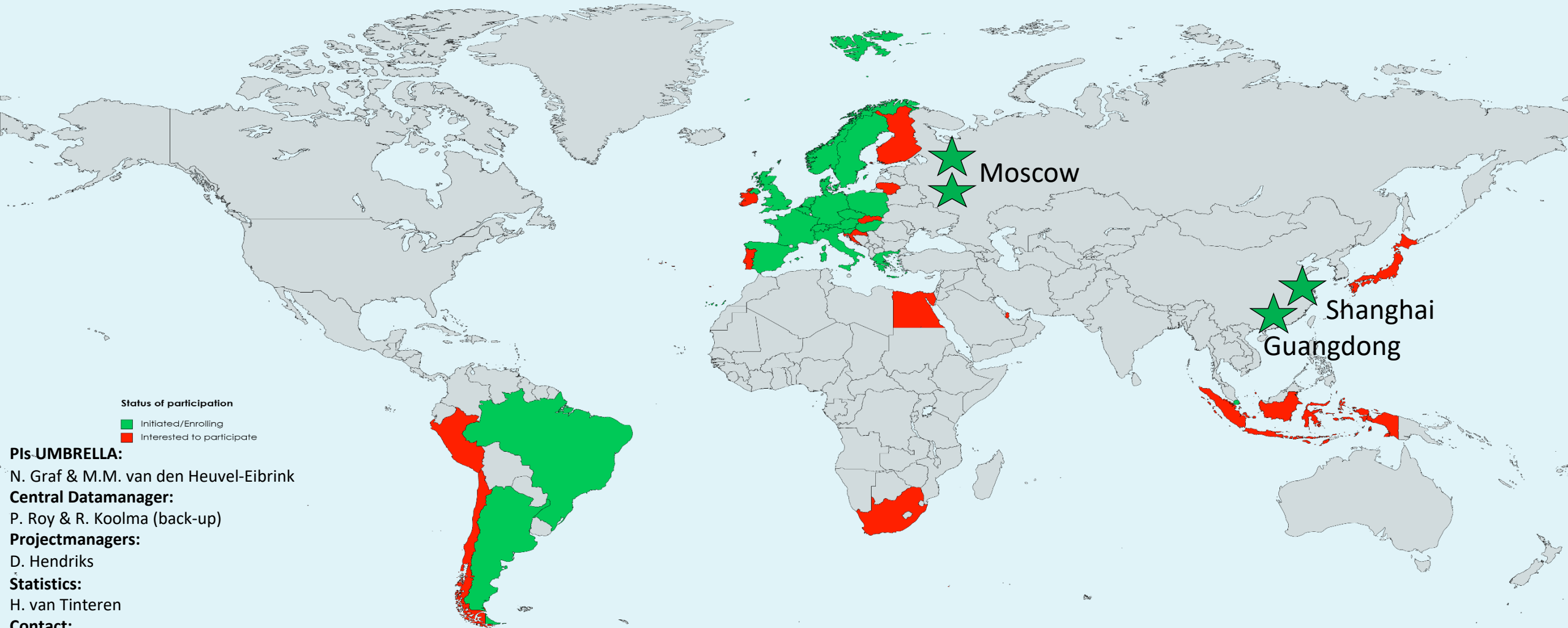


UMBRELLA PROTOCOL

SIOP-RTSG 2016



Newsflash #35
June 2022



PIs-UMBRELLA:
N. Graf & M.M. van den Heuvel-Eibrink
Central Datamanager:
P. Roy & R. Koolma (back-up)
Projectmanagers:
D. Hendriks
Statistics:
H. van Tinteren
Contact:
SIOP-UMBRELLA-dm@prinsesmaximacentrum.nl



UMBRELLA: newsflash June 2022 Participating (as of the 30th of May 2022)

	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
21	Czech Republic	X	X	X	23-7-2021	30-03-2022
22	Sweden	X	X	X	14-3-2022	
23	Slovenia	X	X	X	08-4-2022	
24	Argentina	x	x	x	29-04-2022	12-05-2022

UMBRELLA: newsflash June 2022 Preparing initiation

(as of the 30th of May 2022)



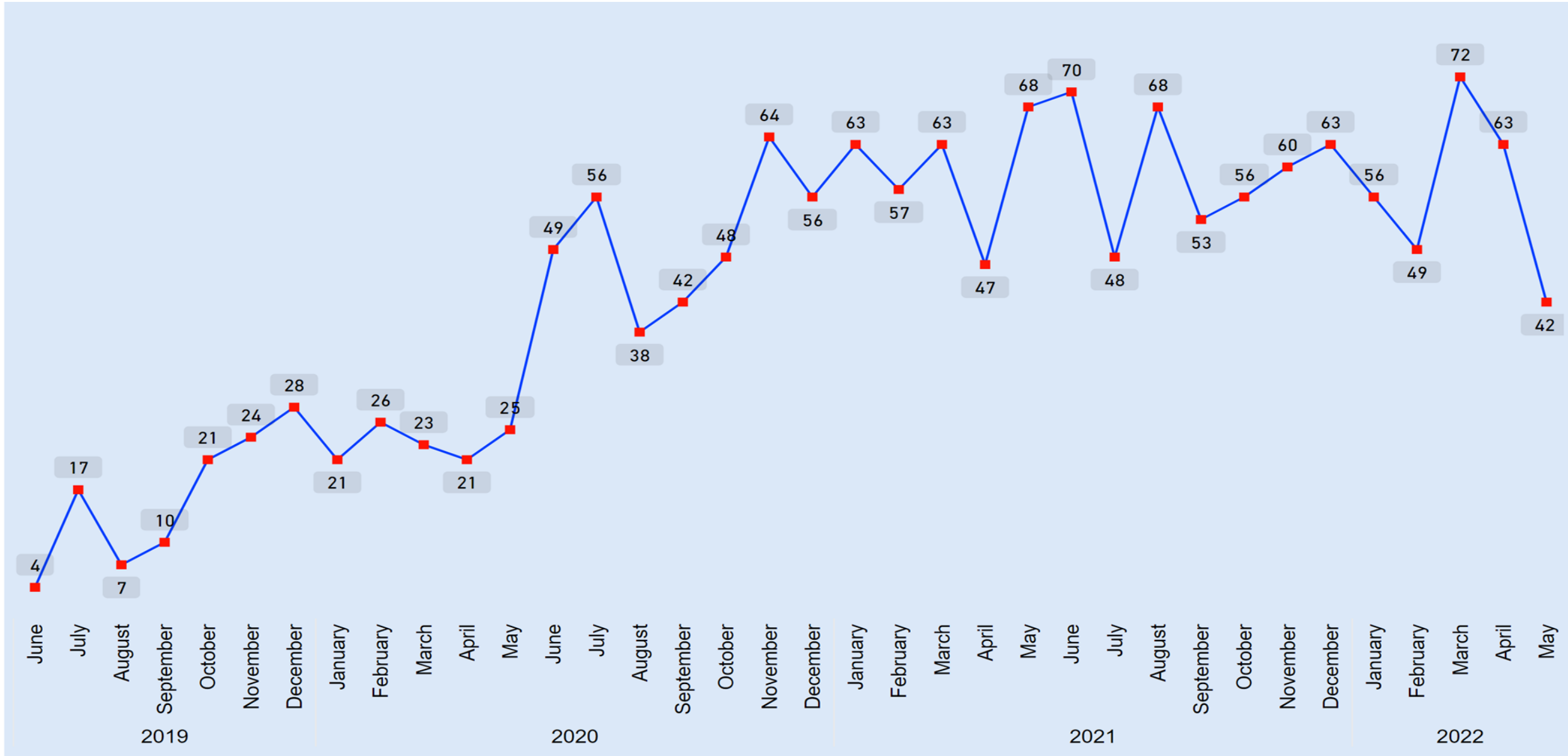
	Countries	Upload names in SIOP-RTSG website	Ethical approval	NCC contract with sponsor	Initiation visit by the SIOP RTSG office
25	Chile				
26	Croatia				
27	Egypt				
28	Finland				
29	Hongkong	Completed	Completed	Completed	CIV pending by request Hong Kong (june 2022)
30	Indonesia				
31	Ireland	Completed	Pending	Pending	
32	Japan	Completed	Completed	Pending	
33	Lithuania	Completed	Completed	Under review	
34	Portugal				
35	Peru	Completed			
36	Qatar				
37	Slovakia				
38	South Africa				
39	Australia				
40	Latvia				

*) CIV is Country initiating visit

UMBRELLA: total enrolment per month

(as of the 28th of April 2022)

Total enrolment= 1578 (ALEA) + 27(ObTima)

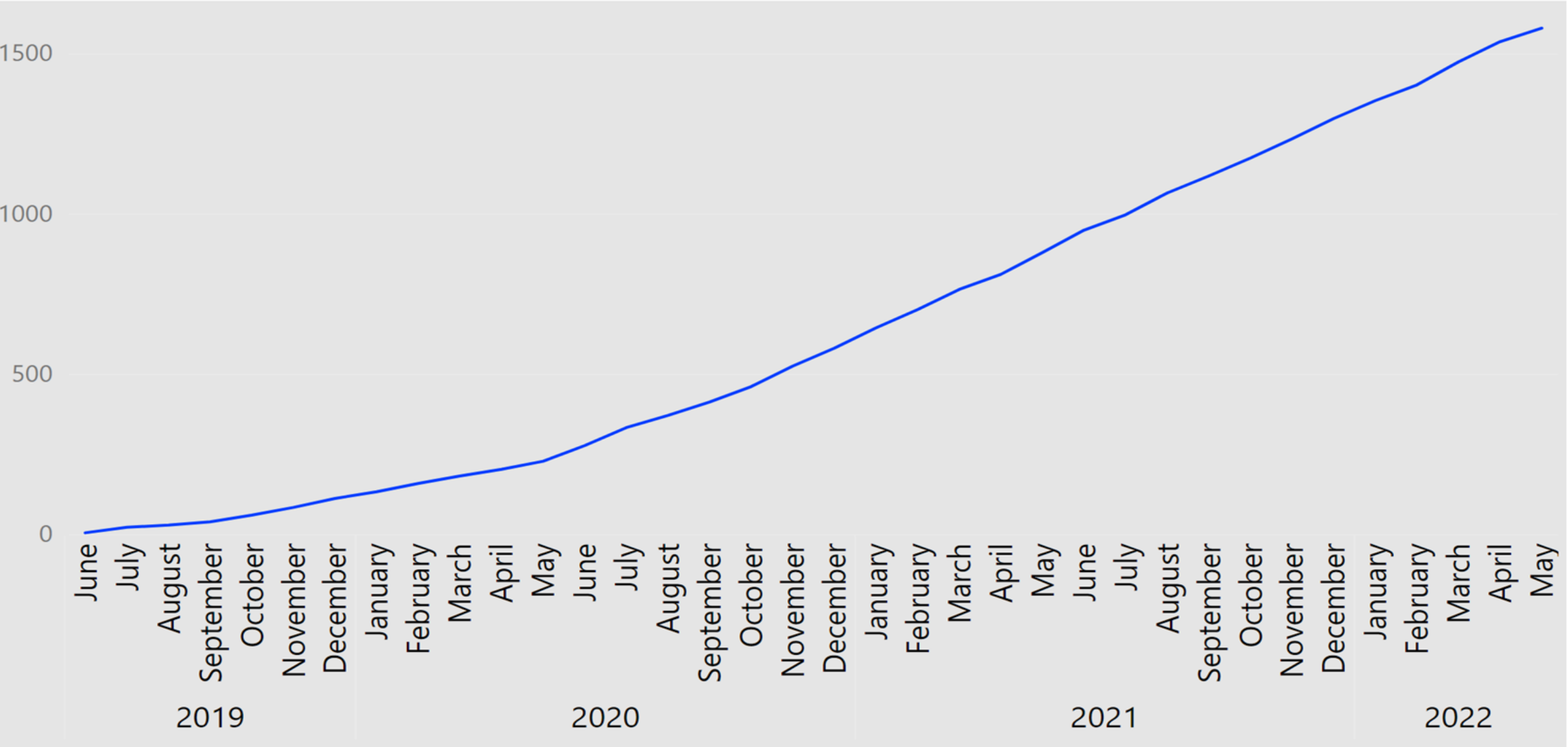


UMBRELLA: cumulative incidence

(as of the 30th of May 2022)



Total enrolment= 1605



UMBRELLA: country specific enrolment

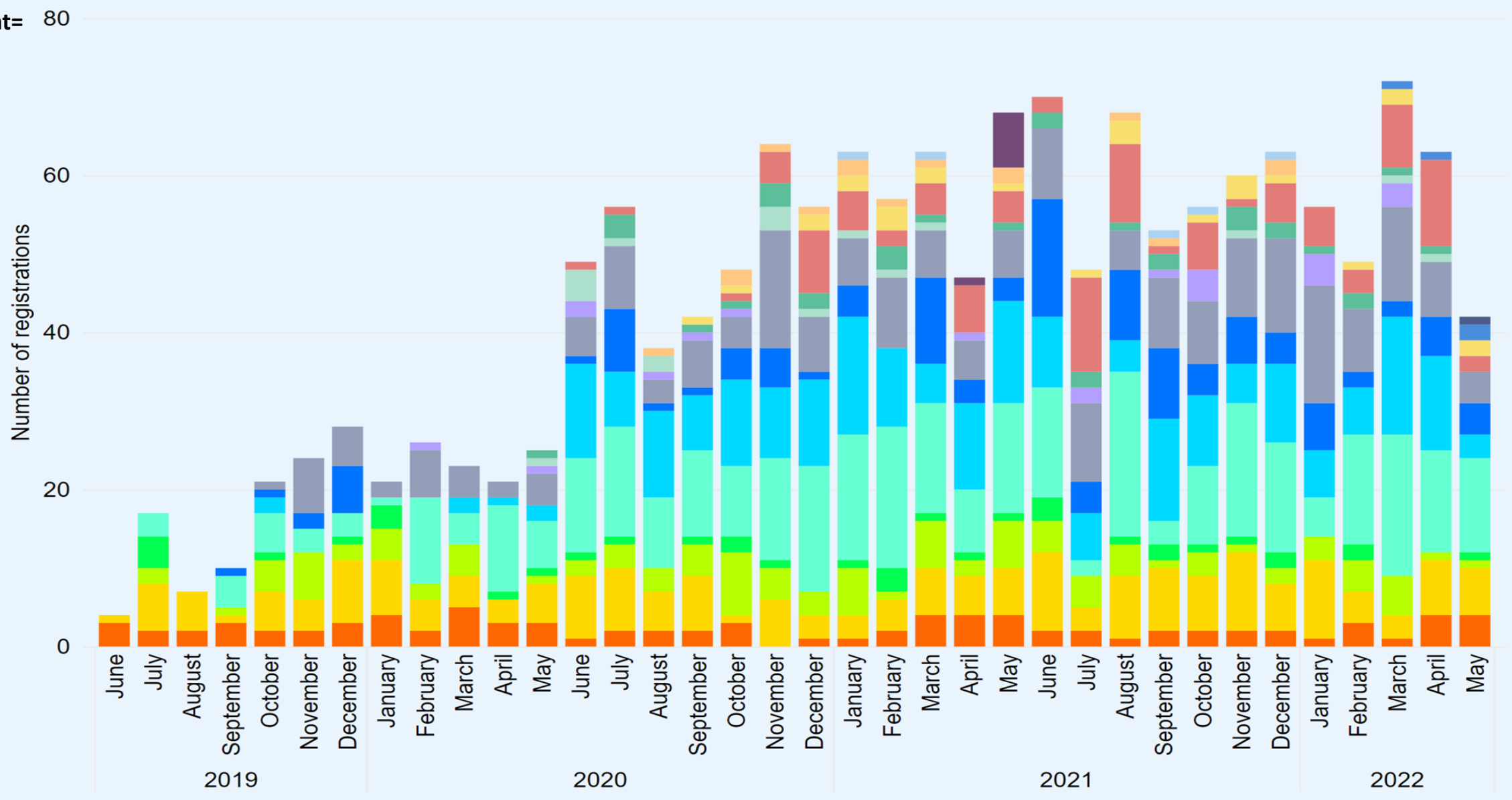
(as of the 30th of May 2022)



Total enrolment= 80
1605

Country Name

- Netherlands
- Italy
- Spain
- Greece
- Brazil
- France
- China
- UK
- Norway
- Denmark
- Switzerland
- Russia
- Belgium
- Hungary
- Singapore
- Poland
- Czech Republic
- Argentina



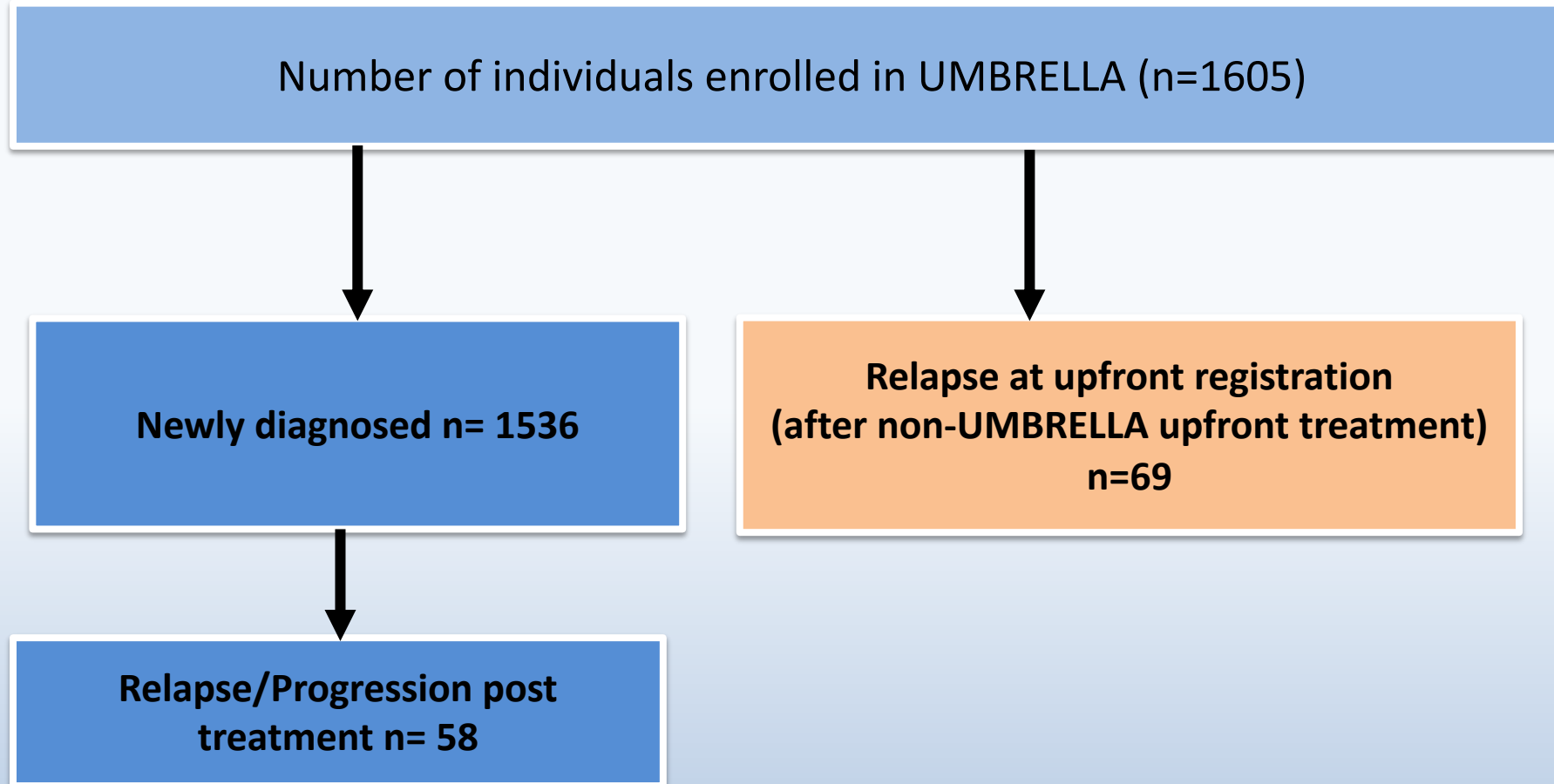
UMBRELLA: monthly enrolment per national/regional sites

(as of the 30th of May 2022)



	Austria	Belgium	Brazil	Czech Republic	Denmark	France	Greece	Germany	Hungary	Italy	Netherlands	Norway	Poland	Singapore	Spain	Switzerland	UK	China-01	China-02	Russia-01	Russia-02	Grand Total
2019 Total			18			2	6			30	17				15		13	10				111
2020 Total		4	117		12	73	11		5	61	28	7			38	11	66	7	14	5	10	469
January		2	16		1	15	1		2	3	1			1	6		6		4	1	4	63
February		3	18		1	10	3		1	4	2				1	3	9			2		57
March		2	14		1	5	1		1	6	4			1	6	1	6	7	4	1	3	63
April			8			11	1			5	4	1	1		2		5		3	3	3	47
May		1	14			13	1		2	6	4		7		6	1	6		3		4	68
June			14			9	3			10	2				4	2	9	12	3		2	70
July	1	1	2			6		1		3	2	2			4	2	10		4	10	2	48
August	0	3	21			4	1	0	1	8	1				4	1	5		9	4	6	68
September	0		3			13	2	0	1	8	2	1		1	1	2	9	6	3	1		53
October	0	1	10			9	1	0		7	2	4		1	3		8		4	4	2	56
November	0	3	17		1	5	1	1		10	2	0	0		1	3	10		6		1	58
December	1	1	14		0	10	2	2	2	6	2	0	0	1	2	2	12	1	3	3	2	
2021 Total	2	17	151		4	110	17	4	10	76	28	8	8	5	40	17	95	26	46	29	29	722
January	0	0	5		0	6	0	3	0	10	1	4	0	0	3	1	15	3	3	4	1	59
February	0	1	14			6	2	6	0	4	3	0	0	0	4	2	8	0	2	0	3	55
March	0	2	18	1	1	15	0	4	0	3	1	3	0	0	5	1	12	0	2	6	2	72
April	0	0	13	1	1	12	0	3	0	7	4	0	0	0	1	1	7	0	5	6	4	0
May	0	2	12	2	0	3	1	5	0	6	4	0	0	0	1	0	4	0	4	0	2	
Grand Total	2	26	348	4	18	227	37	25	15	197	86	22	8	5	107	33	220	46	76	50	52	1578

Enrolment UMBRELLA



Of the patients with completed national reference pathology review(F15), 1016 , n=190 were non-WT (18.7%)

Biobanking Informed consent(F0)(total no =1578) vs F5 (total no= 756) available



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

SIOP-RTSG-UMBRELLA: what's new?

Inclusion summary:

- 24 National/Regional Coordinating Centres initiated, 22 enrolling
- Total enrolment: 1578+22 patients
- [Argentina, Slovenia](#) have been initiated in [April 2022](#)
- [Hong Kong](#) is planned for [June \(2022, delay because of COVID-19\)](#)
- [Ireland, Croatia, Lithuania](#) are in the final phase before country initiation, now.
- Inclusion is steadily moving, but due to Corona crisis(still relevant for instance in Asia and South-America), we anticipate that some registration delays still may occur. Nevertheless, **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)



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)
- 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)

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 is open in Germany now!** (Stage IV, RCT), PI: A Verschuur and R Furtwangler
- The **miRNA study** by Eckart Meese is launched
- Please (encourage all your co-workers to) become members of SIOP-RTSG. The application form can be found on the <http://siop-rtsg.org> website.



An amendment of the UMBRELLA protocol is prepared by the steering committee

Content:

- 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 NBL 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)

The amended document is sent for ethical approval by the sponsor. As soon as it is approved, this will be announced and the emended version will be placed on the SIOP-RTSG website