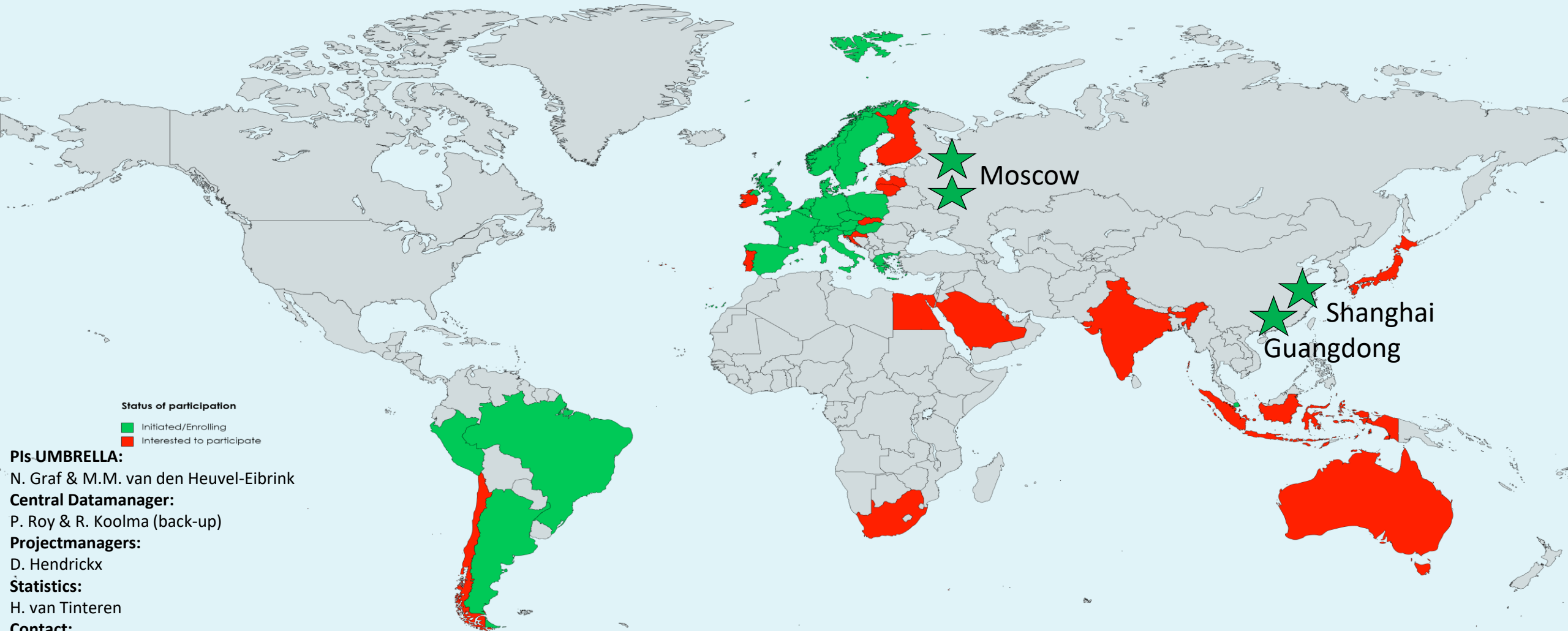


UMBRELLA PROTOCOL

SIOP-RTSG 2016



Newsflash #41
January 2023



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UMBRELLA: newsflash January 2023 Participating (as of the 28th of Dec 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



UMBRELLA: newsflash January 2023 Participating (as of the 28th of Dec 2022)

#	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	
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	

UMBRELLA: newsflash January 2023 Preparing initiation

(as of the 28th of Dec 2022)



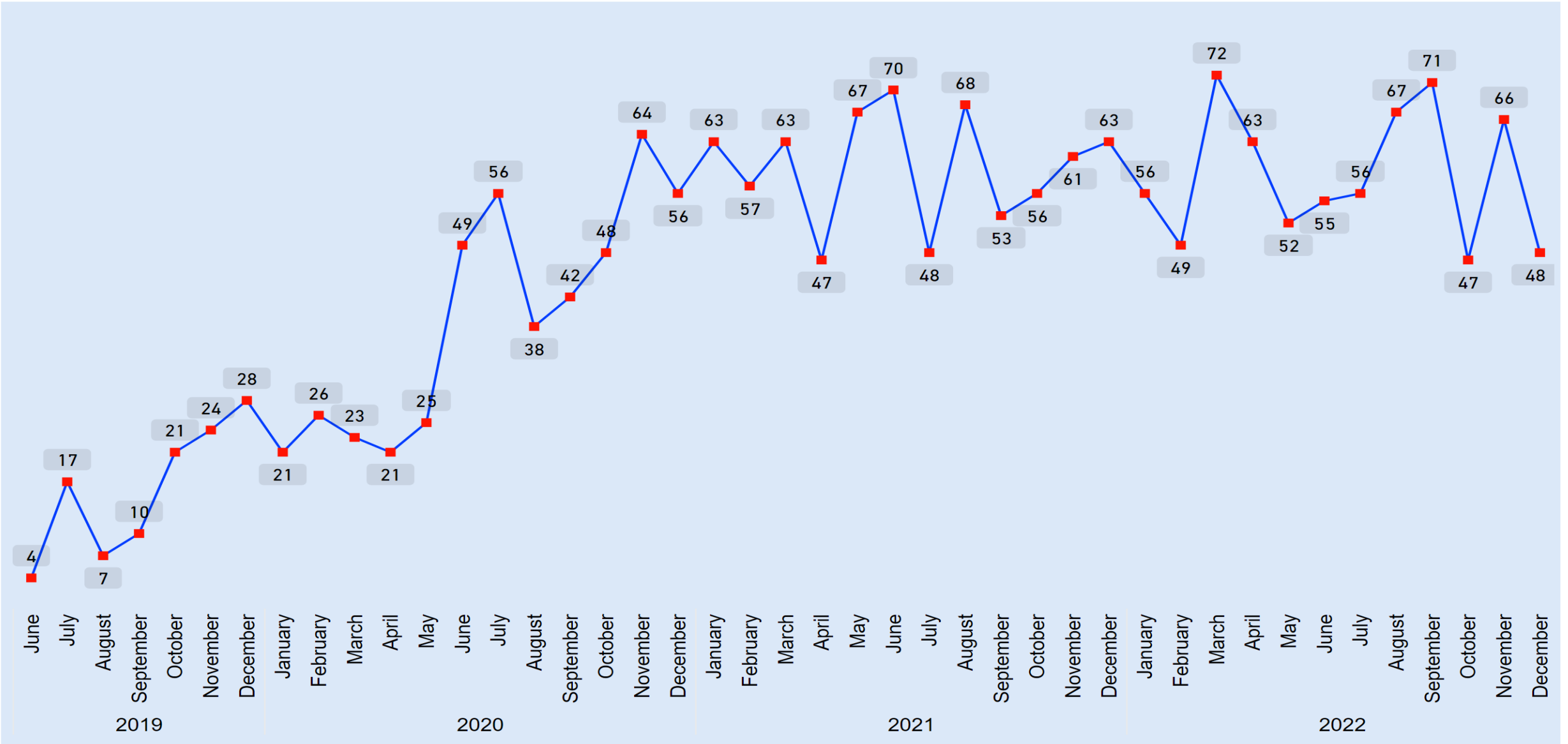
	Countries	Upload names in SIOP-RTSG website	Ethical approval	NCC contract with sponsor	Initiation visit by the SIOP RTSG office
27	Chile				
28	Croatia				
29	Egypt	Pending	Pending	Pending	
30	Finland				
31	Hongkong	Completed	Completed	Completed	CIV pending by request Hong Kong due to COVID
32	Indonesia				
33	Ireland	Completed	Pending	Pending	
34	Japan	Completed	Completed	Completed	CIV scheduled for 25 JAN 2023
35	Lithuania	Completed	Completed	Under review	
36	Portugal				
37	Qatar				
38	South Africa				
39	Australia				
40	Latvia	Completed	Completed		
41	Saudi Arabia				
42	India				

*) CIV is Country initiating visit

UMBRELLA: total enrolment per month

(as of the 28th of Dec 2022)

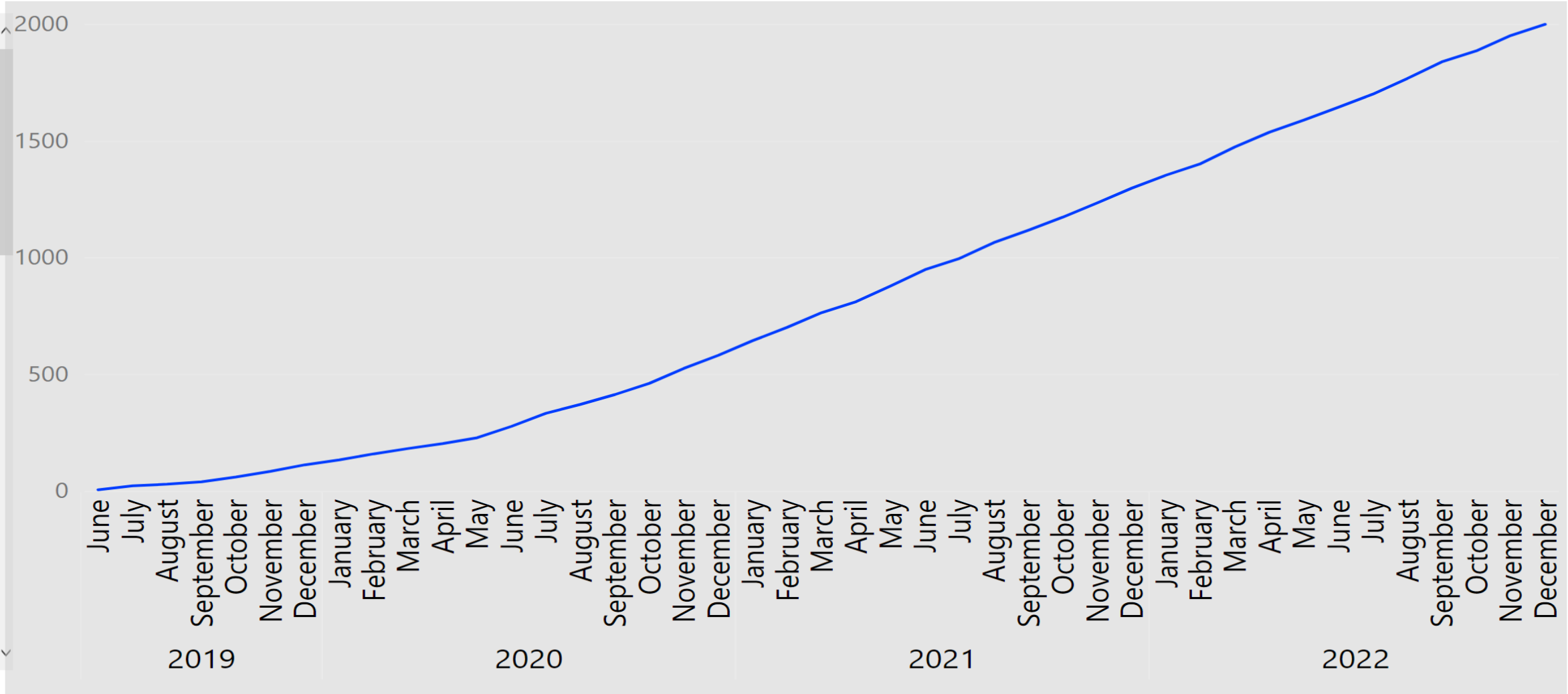
Total enrolment = at least 2077



UMBRELLA: cumulative incidence

(as of the 28th of Dec 2022)

Total enrollment = at least 2077



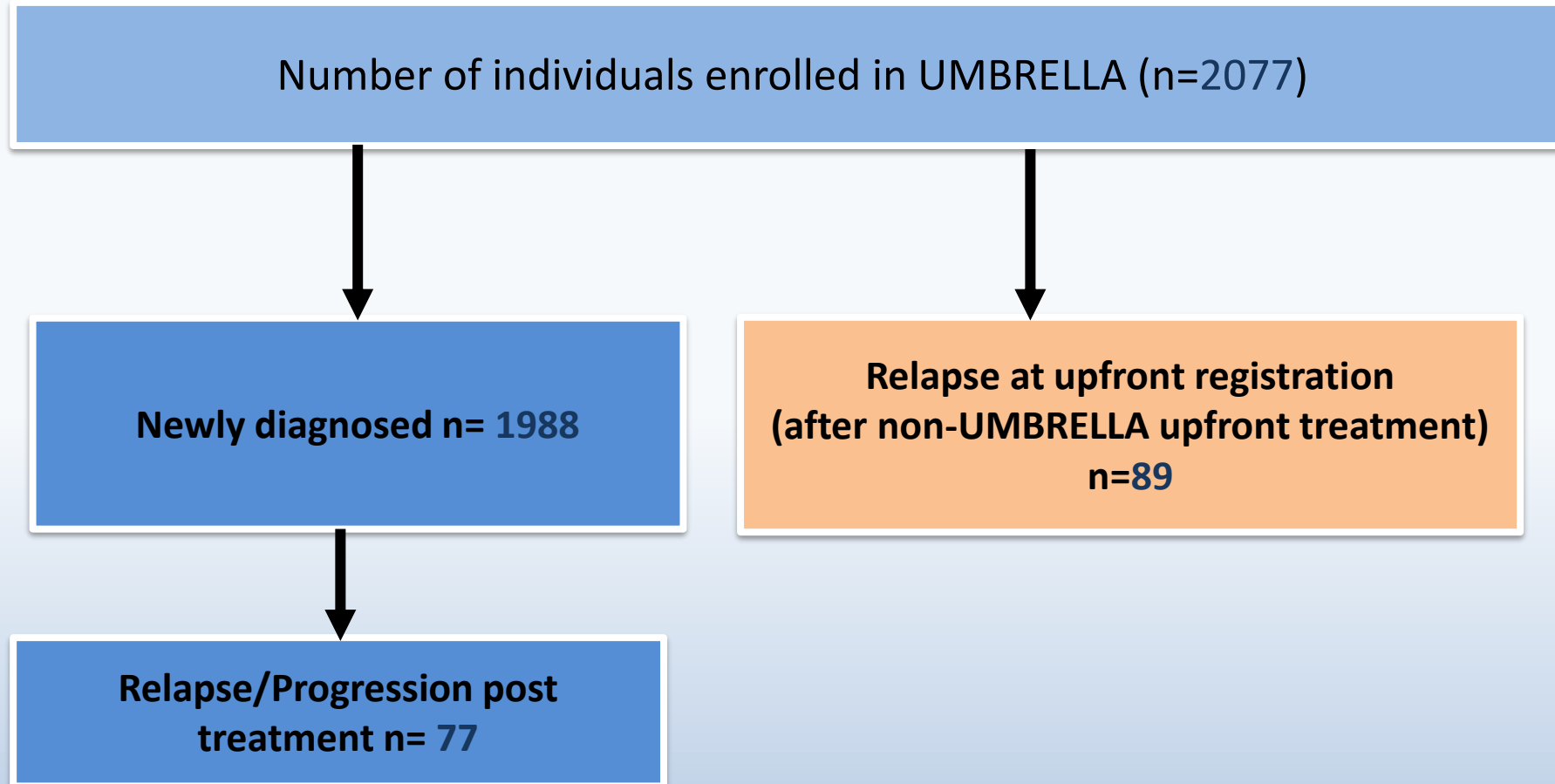
UMBRELLA: monthly enrolment per national/regional sites

(as of the 28th of Dec 2022)



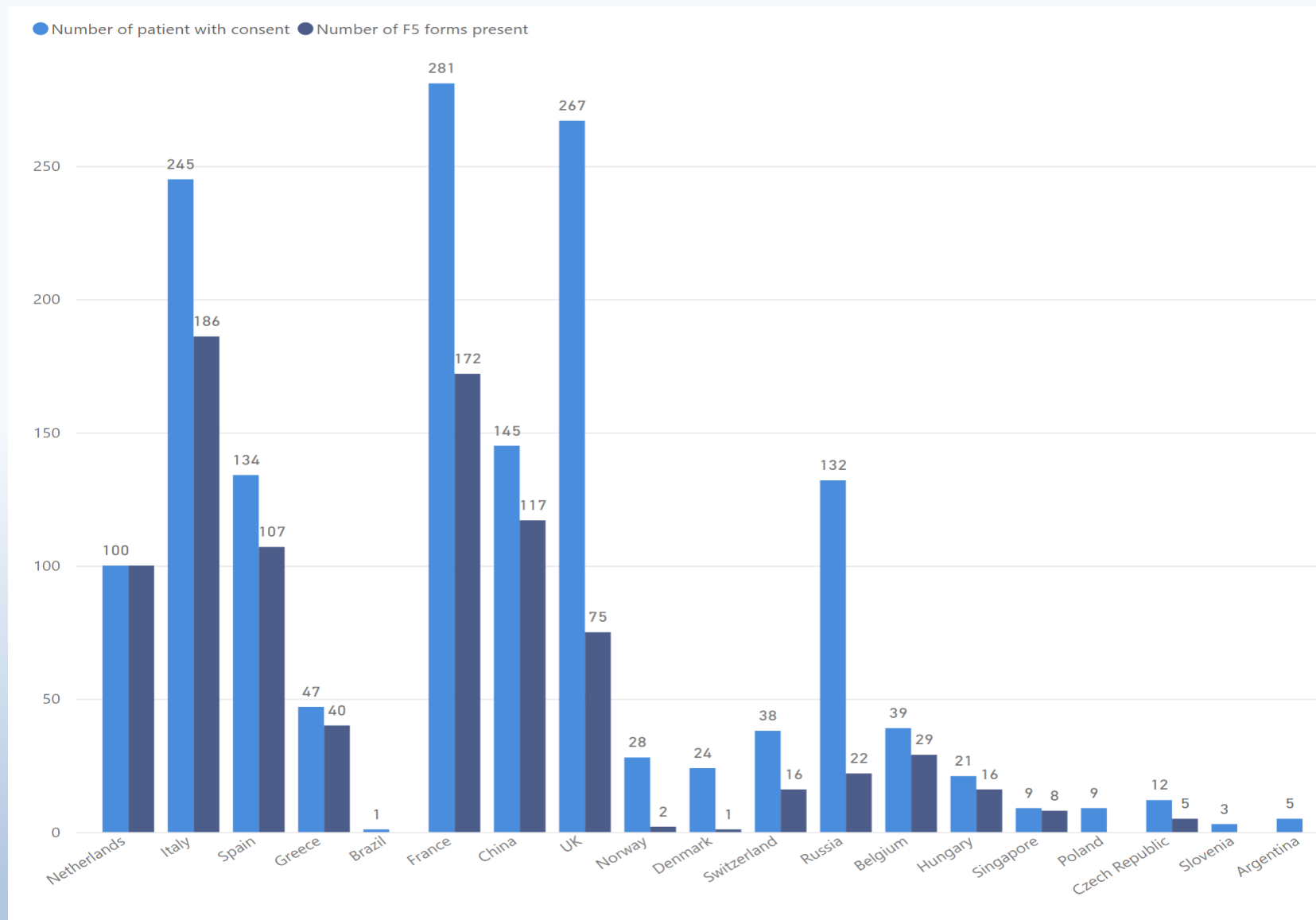
	Argentina	Austria	Belgium	Brazil	Czech Republic	Denmark	France	Greece	Germany	Hungary	Italy	Netherlands	Norway	Poland	Singapore	Slovenia	Spain	Switzerland	UK	China-01	China-02	Russia-01	Russia-02	Grand Total
2019 Total				18			2	6			30	17					15		13	10				111
2020 Total			4	117		12	73	11		5	61	28	7				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			5	1	6		3		4	67
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	50
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	61
December		1	1	14		0	10	2	2	2	6	2	0	0	1		2	2	12	1	3	3	2	66
2021 Total		2	17	151		4	110	17	4	10	76	28	8	8	5		39	17	95	26	46	29	29	721
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		0	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	76
April		0	0	13	1	1	12	0	3	0	7	4	0	0	0		1	1	7	0	5	6	4	65
May	1	0	3	14	2	0	4	1	5	0	7	5	0	0	0		1	0	6	0	3	0	2	54
June	1	0	1	10	1	2	9	2	8	1	7	5	2	0	0		4	1	6	0	4	0	2	66
July	1	0	2	8	0	0	10	1	13	0	9	5	2	0	0		3	0	9	0	2	1	3	69
August	0	0	1	17	0	2	5	2	7	1	6	2	1	0	0	1	4	1	6	0	7	5	6	74
September	0	0	4	9	3	1	9	0	7	2	12	2	0	1	1	0	4	3	7	5	1	4	3	78
October	1	0	3	0	1	1	10	2	5	0	7	2	0	0	1	0	6	1	6	0	2	1	2	51
November	1	0	0	22	0	1	8	3	11	2	4	0	1	0	2	2	3	2	4	0	3	3	5	74
December	0	tba	1	13	3	1	4	2	tba	0	4	1	0	0	0	0	6	2	8	0	0	0	3	48
Grand Total	5	2	39	429	12	26	285	49	76	21	247	104	28	9	9	3	136	43	268	51	94	64	76	2076

Enrollment UMBRELLA



Of the patients with completed national reference pathology review(F15), n=1190 , n=213 were non-WT (17.9%)

Biobanking Informed consent(F0)(total no =1540) vs F5 (total no= 896) available



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

SIOP-RTSG-UMBRELLA: what's new?

Inclusion summary:

- 26 National/Regional Coordinating Centres initiated, 23 enrolling
- Total enrollment: at least 2077 patients
- Slovakia has been initiated in October 2022, Japan will be initiated in January 2023.
- Initiation of Hong Kong is expected soon (delay because of COVID-19)
- Ireland, Latvia, Lithuania are in the final phase before country initiation now.

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)



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 now!** (Stage IV, RCT), PI: 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 SIOP-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.

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)