IR HIGH

	Induction (NCI High Risk/T-cell)																												
Week	1							2							3							4							
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Dexa 6 mg/m²																													
VCR 1.5 mg/m²																													
DNR 25 mg/m²																													
PEG-Asp 1500/1000 IU/m²				1														2											
ITT, according to age								*														*							
	*CNS2/3 and TLP+																												
BM	x														x														x

TREATMENT PHASE	**DURATION**	**DETAILS OF TREATMENTS/ RANDOMISATIONS**
Consolidation 1	6 weeks (weeks 5-10)	
Consolidation 2	7 weeks (weeks 11-17)	
Delayed Intensification	12 weeks (weeks 18-29)	
Consolidation 3	7 weeks (weeks 30-36)	
Maintenance	Continues for exactly 2 years from the start of consolidation 1 (+6 weeks for patients in the InO-arm)	Randomisation 3. 2-way (InO+SM vs SM) See below

	IR-High Consolidation 1																																									
Week	5							6							7							8							9							10						
Day	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
Dexa																																										
VCR 1.5 mg/m²																																										
6-MP 60 mg/m²																																										
ARA-C 75 mg/m²																																										
PEG-Asp 1500/1000 IU/m² TDM				3														4														5										
CPM, 1000 mg/m²																																										
IT according to CNS/age																																										
BM	x																																									

	IR-High Consolidation 2																																																						
Week	11							12							13							14							15							16							17							
Day	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119
6-MP 25 mg/m²																																																						
MTX 5000 mg/m²																																																						
PEG-Asp 1500/1000 IU/m² TDM				6														7														8																					
IT according to CNS/age																																																						
BM	X																																																					

	IR-High Extended Delayed Intensification																			
Week	18 (21, 24, 27)							19 (22, 25, 28)							20 (23, 26, 29)					
Day	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140
Dexa 10 mg/m²																					
VCR 1.5 mg/m²																					
DOX 30 mg/m²																					
6-MP 50 mg/m²																					
IT according to CNS/age																					

Eligible patients:
IR-high stratification.

This phase runs for 12 weeks from day 120 (beginning of week 18) to day 203 inclusive (end week 29) in cycles of 3 weeks each.

	IR-High Consolidation 3																																																						
Date																																																							
Week	30							31							32							33							34							35							36							
Day	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252
6-MP 25 mg/m²																																																						
MTX 5000 mg/m²																																																						
IT according to CNS/age																																																						

ALLTogether

	IR-High Maintenance with VCR-Dexa pulses																												
Week	37							38							39							40							
Day	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	etc
6-MP 75 mg/m^2																													
MTX 20 mg/m^2																													
IT according to CNS/age	*																												
VCR 1.5 mg/m^2																													
Dexa 6 mg/m^2																													
*Every 3rd cycle (every 12 weeks) throughout Maintenance																													

ELLER hvis randomiseret til InO i R3

	IR-High Inotuzumab experimental arm																																									
Week	37							38							39							40							41							42						
Day	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294
InO 0.5 mg/m^2																																										
	Cycle 1																					Cycle 2																				

	IR-High Maintenance with VCR-Dexa pulses post InO																												
Week	43							44							45							46							
Day	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	etc
6-MP 75 mg/m^2																													
MTX 20 mg/m^2																													
IT according to CNS/age	*																												
VCR 1.5 mg/m^2																													
Dexa 6 mg/m^2																													
*Every 3rd cycle (every 12 weeks), throughout Maintenance																													

Eligible patients:

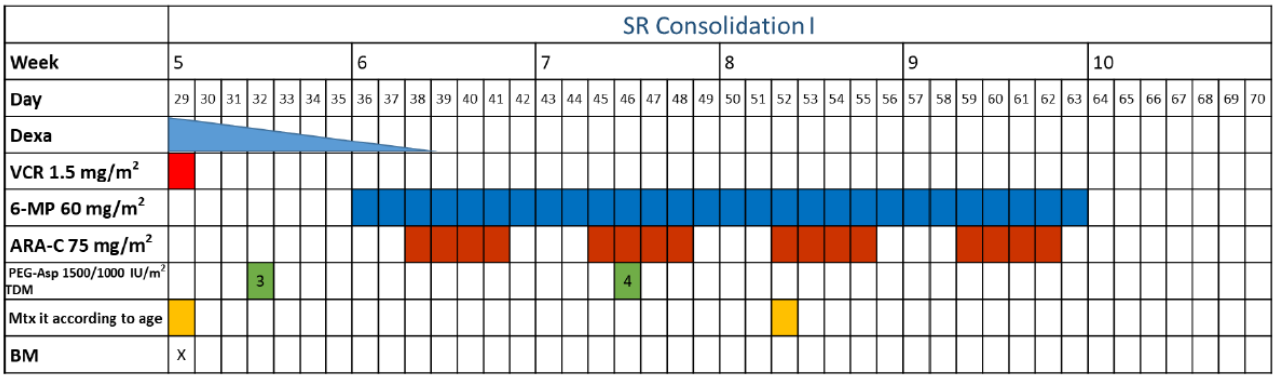
This part of the protocol applies to

- Patients who have received the experimental Inotuzumab block and should continue Standard Maintenance.

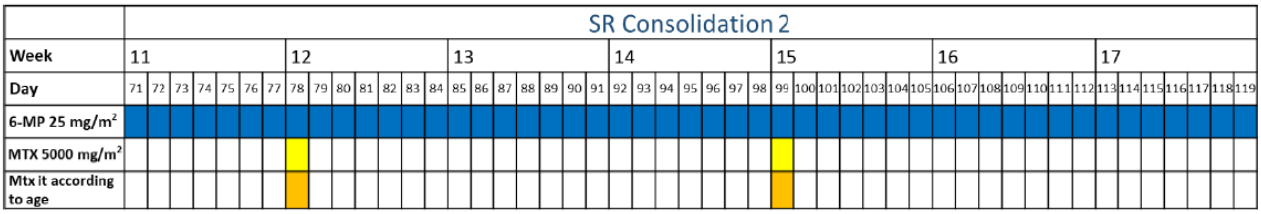
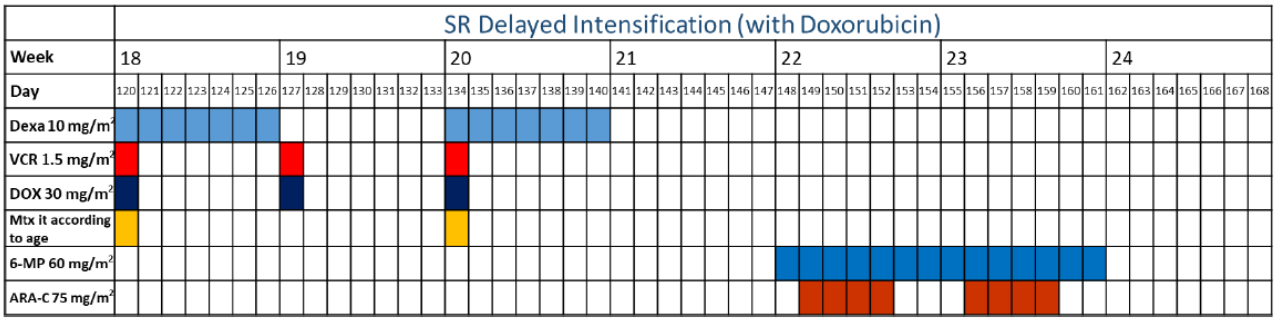
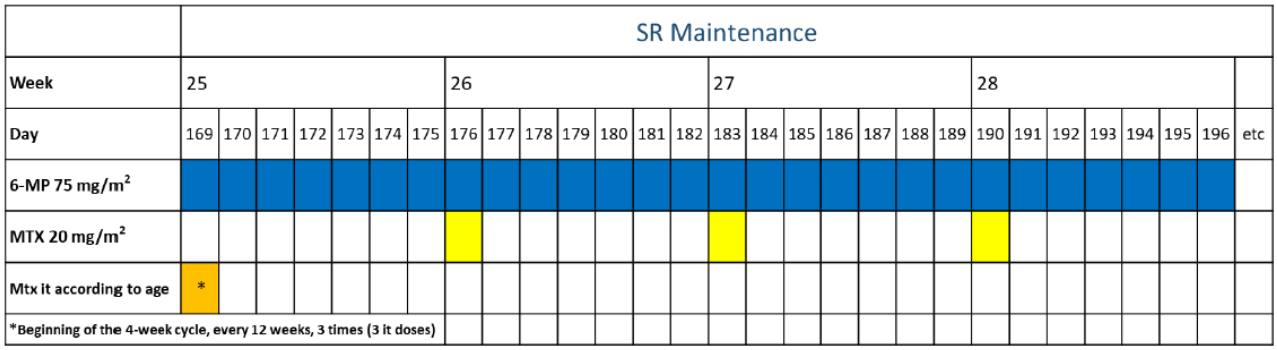
Standard Risk

	Induction (NCI High Risk/T-cell)																											
Week	1							2							3							4						
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Dexa 6 mg/m^2																													
VCR 1.5 mg/m^2																													
DNR 25 mg/m^2																													
PEG-Asp 1500/1000 IU/m^2				1														2											
ITT, according to age								*														*							
	*CNS2/3 and TLP+																												
BM	x														x														x

TREATMENT PHASE	DURATION	DETAILS OF TREATMENTS/RANDOMISATIONS
Consolidation 1	6 weeks (weeks 5-10)	
Consolidation 2	7 weeks (weeks 11-17)	
Delayed Intensification	7 weeks (weeks 18-24)	Randomisation 1. With and without Anthracycline (Doxorubicin)
Maintenance	Continues for exactly 2 years from the start of consolidation 1	



BM examination for stratification will be performed on day 29 (TP1)

Eligible patients:
This protocol is used for SR-stratified patients.

SR-patients fulfil all the following criteria:
- no detectable MRD-signal at day 29
- BCP-ALL (no T-cell)
- no HR-genetics/ABL-class fusions (for definition see Table 9)
- no CNS3 or TLP+ at diagnosis