Screening phase	PART I: Standard of care:		PART II: Immunotherapy			Follow-up* (most important
	Oligo - SABR Poly - (SAB)R		(x6 cycles)			timepoints showed)
C and E-arm	Day X + 1-14days (depends on total fx)	Last day <u>Friday</u> (72h max before Immuno.)	Day Y +3 ( <u>Monday</u> ) // Y+24 days // +45 // +66 // +87 // +108	Day Y +5 ( <u>Wednesday</u> ) // Y+26 days // +47 // +68 // +89 // +110	Day Y + 7 ( <u>Friday</u> ) // Y+28 days // +49 // +70 // +91 // +112	Start counting at randomisation day (R)
Before trail inclusion (min1- 5days)	Start study	Day *Y	Day Y + 3	Day Y + 5	Day Y + 7	Day R+12wks
Eligibility: known inclusion/exclusion criteria,		Last (SAB)R fx	<u>Pre-injection</u>	<u>Pre-injection</u>	<u>Pre-injection</u>	QOL +WHO + adverse events
(SAB)R, aPD(L)1 maintenance?		Follow-up visit	Blood tests	#Blood tests	#Blood tests	CT-scan
Day 1	Day X		WHO	QOL + WHO	WHO	
Informed consent Demographics, medical history, physical examination, vital signs (BP, P, T) height and body	Start (SAB)R fx(n)	! Blood for translational research	Concurrent therapy & medication, PCM 1gr 1h prior, weight	Concurrent therapy & medication, PCM 1gr 1h prior	Concurrent therapy & medication, PCM 1gr 1h prior	! Blood for translational research
weight. Assessment of concurrent therapy. Blood sampling (incl pregnancy test) Histology, collection of stratification factors, SOC	Day X + <14 Follow-up visit (can be the same as on day Y)	(in case of allocation to arm E this bloodsample can be taken together with the bloodtest on first	During-3h-injection: Infusion cycle 30min (BP, T, HR, BR), Adverse events	During-3h-injection: Infusion cycle 30min (BP, T, HR, BR), Adverse events	During-3h-injection: Infusion cycle 30min (BP, T, HR, BR), Adverse events	Day R + ~18wks (Tumour response evaluation (>4weeks after last day cycle 6))
baseline imaging (<6w).  Evaluation of adverse events  Investigator decision ECG+LVEF		injection day)	Post-injection: Infusion cycle (BP, T, HR, BR) at 30min, 1h and 2h, Adverse events	Post-injection: Infusion cycle (BP, T, HR, BR) at 30min, 1h and 2h, Adverse events	Post-injection: Infusion cycle (BP, T, HR, BR) at 30min, 1h and 2h, Adverse events	QOL +WHO + adverse events CT-scan:CR/PR/SD/PD
Day 3- ~8 (signed informed consent and Eligible conform in&exclusion)  Randomisation ( R )						Day R + 24wks  CT-scan  QOL +WHO + adverse events  ! Blood for translational research
E-arm>> Plan Planning CT >> Start developing irradiation plan						Day R + 36wks CT-scan
Translational blood Stool sample + optional biopsy + archived biopsy				QOL +WHO + adverse ! Blood for translational research		
Baseline <b>QOL</b> , Baseline WHO						Day R + 48wks //+54wks //+62wks //+70wks //+78wks QOL +WHO + adverse events
Irradiation plan finished						CT-scan

## Legend - C an E-arm

X: Day were first fx of SABR will be given Y: Last day of the last fx of SABR

**R:** Day were randomisation took place

CR: Complete response; disappearance all target and non-target lesions & normalization of tumour markers

PR: Partial response; at least a 30% decrease in target lesions, Non target lesions non-PD SD: Stable disease

<u>PD:</u> Progressive disease; at least a 20% increase and/or new lesions

**QOL:** Quality of life questionnaires (C30, LC13 and EQ5D)

#Blood tests: blood test is only planned if it is the investigator's decision.

\* Be aware that only most important time points are presented. Other time points e.g. 6wks interval (if SOC) are not shown.

Be aware: E-arm patients will receive FUscans (incl contrast) during L19-IL2 cyclus. FU-scans 1.5 weeks after L19-IL2 infusion but befor start new cycle!

BP: blood pressure, ECG: electrocardiogram, fx: fractions, gr: gram, h: hour, HR: heart rate, LVEF: left ventricular ejection fraction, P: puls, R: randomisation, T: temperature, WHO: world health organization Performance Status, wks: weeks.