B.6 Follow-up

The follow-up starts with the day of the final ophthalmological examination at the end of treatment or the day of enucleation. The following examinations are recommended to be performed at predefined time points until the age of 18.

- indirect ophthalmological EUA, including
    - tonometry
    - inspection of the anterior chamber
    - palpation of the orbita after enucleation
    - if changes have occurred, ultrasound and RetCam imaging
    - documentation of regression patterns of the previously treated retinoblastoma
- age-appropriate test of visual acuity (PL or BCVA)
- medical history and general physical examination by a pediatric oncologist. Evaluation of
    - development
    - onset of puberty
    - fertility
    - incidence of second primary malignancies
- dental examination (all children especially those that received radiotherapy including brachytherapy)
    - incidence of odontogenic malformations in the radiation field
    - incidence of karies
- diagnostic evaluations for patients **after chemotherapy,** including
    - blood tests (including U+E, creatinine, LFTs) to evaluate renal and hepatic toxicity, if appropriate
    - hearing test to evaluate ototoxic effects of platinum compounds
- assessment by a radiation oncologist for children that received **EBRT or brachytherapy**

B.6.1 Patients without *RB1* germline mutation

Patients not harboring germline *RB1* mutations, who received globe-salvaging treatment for IRSS stage 0 retinoblastoma, require regular (at least every 6 months) ophthalmological examinations until 5 years of age. After enucleation of the affected eye and no further therapy (IRSS stage I N0, N1, C0, C1, S0) ophthalmological inspection should be performed at least once yearly until 5 years of age. Patients with IRSS stage I/II N2, C2, S2, S3, III, IV require ophthalmological and pediatric oncological follow-up every 3 months for the first year and every 6 months until 5 years of age. Pediatric oncological examination should be performed in all children at least once yearly until 5 years of age.

At 6 years of age, all patients in RB-Registry should receive a test of visual acuity, a hearing assessment, a pediatric oncological examination with a focus on late effects and an assessment of quality of life.

Table B-3: Follow-up examination for nonheritable retinoblastoma

Required investigations	**< 5th yr of age**	**> 5th yr of age**
Ophthalmological evaluation		
indirect ophthalmoscopy	at least every 6 months (EUA)	every 2 yrs
analysis of vision	1x/ yr	
Pediatric assessment		
physical examination with anthropometric parameters	1x/ yr	every 5 yrs
vaccination	revaccinate according to local guidelines [C]	
Blood tests		
liver function tests	1x/ yr [C]	every 5 yrs [C]
creatinine, urea and electrolytes	1x/ yr [C]	every 5 yrs [C]
Radiotherapeutic follow-up [RT]		
clinical examination		age 5, 10, 15 yrs [RT]
dental examination	2x/yr	2x/yr
Other investigations		
audiogram / OAE	1x/ yr [C]	every 5 yrs [C]
Quality of life		
questionnaire for parents and for patients		at the age of 6 yrs

[C] only after chemotherapy; [RT] only after radiotherapy including brachytherapy
ECG, electrocardiogram; EUA, Examination under Anesthesia; OAE, otoacustic emissions

B.6.2 Patients with *RB1* germline mutations

During the first year of life, EUA should be performed at least every 2 months in all children carrying a *RB1* germline mutation (familial or early diagnosed sporadic retinoblastoma). EUA are conducted at least every 4 months in the second year and at least every 6 months during third through fifth years of age (Table B-4). Pediatric oncological examination should be performed in all children at least 1x/year. All children that received radiotherapy including brachytherapy should be seen by a radiation oncologist at the age of 5 years, 10 years and 15 years.

At the age of 6 years, all patients registered on RB-Registry receive a test of visual acuity, a hearing assessment, a pediatric oncological examination with a focus on late effects and an assessment of quality of life.

Table B-4: Follow-up and screening examination for heritable retinoblastoma or mutation status unknown

Required investigations	**1st yr of age**	**2nd yr of age**	**3rd -< 5th yr of age**	**> 5th yr of age**
Ophthalmological evaluations				
indirect ophthalmoscopy (GA until about 5th year of age)	at least every 2 m	at least every 4 m	at least every 6 m	1x/ yr
analysis of vision	1x/ yr (For RB-Registry at the age of 6 years)			
Radiology				
cranial ultrasound (0-6 months)	at diagnosis			
cranial MRI	at diagnosis			
Pediatric assessment				
physical examination with anthropometric parameters	1x/ yr			
vaccination	Revaccinate according to local guidelines [C]			
Blood tests				
liver function tests	1x/ yr [C]			every 5 yrs [C]
creatinine, urea and electrolytes	1x/ yr [C]			every 5 yrs [C]
Human genetics				
counseling	-			1x at 17thyr
Radiotherapeutic follow-up[RT]				
clinical examination				age 5, 10, 15 yrs
dental examination	2x/yr			2x/yr
Other investigations				
audiogram / OAE**	1x/yr [C]			every 5 yrs [C]
Quality of life				
questionnaire for parents and for patients	-			at 6 yrs

[C] only after chemotherapy; [RT] only after radiotherapy including brachytherapy
ECG, electrocardiogram; GA, general anesthesia; yr, year; m, months; OAE, otoacustic emissions

B.7 Screening for familial retinoblastoma

Neonates with a familial risk of retinoblastoma should receive an ophthalmological examination with or without anesthesia within the first 2 weeks after birth. If inheritance of the mutant *RB1* allele can be excluded by genetic testing, children no longer need to be under intensive ophthalmological surveillance. For the remaining children with a familial risk, ophthalmological EUA is advisable at least every two months for the first year of life, then at least every 4 months in the second year of life and every 6 months until 5 years of age (Table B-4).

A cranial MRI is recommended for children with a germline *RB1* mutation. During the first 6 months of life, children with familial retinoblastoma can be monitored by cranial ultrasound instead of MRI, but abnormal ultrasound results should be confirmed with a cranial MRI. The first cranial ultrasound is recommended within the first 2 weeks of life.