Retinoblastoma online Questions & Answers-Clinical and research experts from SJD Barcelona Children's Hospital

Question: 'The child is in stage E, and the treatment was stopped after three rounds of interventional therapy. After stopping the treatment, the tumor is now just blocked the optic nerve head. And the tumor has been shrinking recently. My question is, is it possible that it is still the optic nerve head in this case?

Answer: If the tumor is blocking the vision of the optic nerve, it is more difficult to be sure of inactivity. When we cannot see the optic nerve, it is more dangerous because any reactivation of the tumor could disseminate through the optic nerve.

Question: Can you tell us the current reliability of the treatment plan of Vitrectomy to remove the tumor?

Answer: The active tumor cannot be removed through vitrectomy; we consider vitrectomy in inactive tumors in case of retinal detachment and good visual prognosis.

Question: What is possible ocular side effect if we doing IAC/laser?

Answer: IAC + Laser is the most usual treatment for the management of RBL. Ocular side effects are unfrequent but can be related to each of the techniques: IAC: vascular occlusions, retinal/vitreous hemorrhage, transient ptosis,... Laser treatment: iris atrophy, cataract, retinal hemorrhage, retinal detachment,...

Question: For grade C RB, is it can be treatment only with local therapy?"

Answer: No, usually group C need chemoreduction, either with systemic or intra-arterial chemotherapy and only thereafter, local treatment is given, we usually don't do vitrectomy in active tumors for the risk of dissemination.

Question: Are there any approved GD2 antibody medicine for retinoblastoma on the market? Is it intravenous infusion, arterial intervention, or vitreous injection? Do you have any experience on usage and dosage, can you share with that?

Answer: There is no immunotherapy formally approved for retinoblastoma by regulatory agencies. However, retinoblastoma express high levels of GD2 and anti-GD antibodies were used by our group and others to treat patients with disseminated extraocular disease. It is given by intravenous infusion. We have treated thus far 2 children with Naxitamab under a compasionate use basis and the initial results were favorable.

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SJD Sant Joan de Déu Barcelona · Hospital

Question: Hi Doctor, after the operation, the pathological results show that the tumor invades the optic nerve, the end. What's the survival rate?

Answer: This is quite unfortunate and there are many variables that influence survival (e.g., if the optic nerve was enlarged in the MRI) but in general, these children need very intensive therapy and overall, the survival rate is around 60-70%

Question: Do you have any tumor removal surgery for Retinoblastoma?

Answer: At this point intraocular surgery for direct tumor removal has been associated with very bad and dangerous results in patients with active tumor in all international centers that have tried. It is still a technique only to be used with investigation purposes, preferably in animals before using it in human patients."

Question: Is it possible to reset the retina and restore vision after retinal detachment treatment?

Answer: If there is a retinal detachment, vision could be restored with the resolution of the retinal detachment. In some cases, the retinal detachment is a sign of tumor activity, in other it happens because there are small retinal tears that need to be closed to solve the retinal detachment.

Question: Is anterior chamber implant treatment convenient? Is it easy to relapse?

Answer: Anterior chamber seeds can be treated in some particular cases: eyes with visual potential without extraocular disease.

Question: The tumor was removed by vitrectomy, and two weeks after the injection of silicone oil, the pupils became enlarged (or) unchanged. What might be the consequences?

Answer: After vitrectomy usually, we use mydriatic and antiinflamatory drops. Pupil dilatation might be for that. If it continues after one or two weeks after discontinuation of drops, it might be other causes: iris ischemia or toxicity or others.

Question: Will arterial intervention cause eyeball atrophy?

Answer: In some cases, IAC can provoke eyeball atrophy but it is a rare event.

Question: I want to hear what the doctor has to say about vitrectomy,

Answer: We do not routinely use vitrectomy at SJD. Some centers are using it, but it is still not known if it is safe. We prefer to try first the treatment with the virus VCN01","At this point intraocular surgery for direct tumor removal has been associated with very bad and dangerous

results in patients with active tumor in all international centers that have tried. It is still a technique only to be used with investigation purposes, preferably in animals before using it in human patients."

Question: Can the tumor be removed for retinoblastoma?

Answer: Only with taking the whole eye out, there is no chance of conservative surgery.

Question: The choroid of the eyeball has shrunk due to intervention. Is there any way to save the choroidal atrophy? Does the choroidal atrophy inevitably lead to the atrophy of the eyeball? Is there any way to relieve the atrophy of the eyeball?

Answer: Once the choroid has shrunk, probably for ischemia secondary to IAC there is no way to recover it. It doesn't mean that the eyeball atrophy will follow, but the ptisis or atrophy of the eyeball can happen in heavily treated eyes and it is very difficult to solve. In some cases, if there is no vision and the second eye is fine, the best option is enucleation both for safety and aesthetics.

Question: It is Macular tumor, and the macular area has been destroyed, Is it possible to recover vision?

Answer: If the macula is destroyed by the tumor or because of the treatment, we can only preserve peripheral vision, but it is also important, because it helps people to navigate and move around.

Question: To what extent will the atrophy of the eyeball affect the development of the orbit? What is the evaluation criteria? How to intervene?

Answer: If the eye has no vision and it is extremely atrophic, in some cases, a good option is the enucleation with orbital implant, that permits better aesthetics.

Question: Do you have any Retinoblastoma tumor removal surgery? Can the tumor be removed for retinoblastoma?

Answer: The active tumor cannot be removed through vitrectomy, We consider vitrectomy in inactive tumors in case of retinal detachment and good visual prognosis.

Question: How many failed cases treated by vcn? Why?

Answer: All eyes treated have had a good response and the VCN virus has been effective inactivating the tumor and preserving the normal retinal cells. Not all the eyes could be preserved, because most of the eyes included in the trial are final stage eyes, just before enucleation.

The experience with the first two patients was promising and we published the data in the journal Science translational medicine in 2019. Such initial data in patients

showed the feasibility of the administration of intravitreous VCN-01. Patients received two doses of VCN-01 (first patient received 1/100 of the maximum feasible dose of the trial, and patient 2 received 1/10 of the maximum feasible dose; thus, none of the patients received the maximum feasible dose, due to the design of the study). Both doses were injected 14 days apart, according to the trial protocol. After virus injection, patients did not present with any systemic complications and viral genomes were not detected in patient blood. Systemic concentrations of neutralizing antibodies increased during treatment, reaching high titer (1:41,000) in patient 2. Retinal fundoscopic photographs prior to and during VCN-01 treatment showed that both patients developed intravitreous inflammation recorded as vitritis after the first administration. In patient 1, vitritis-associated turbidity precluded monitoring the tumor activity and the eye was finally enucleated as per protocol guidelines. Intravitreous inflammation was controlled in patient 2 using corticosteroids (systemic methylprednisolone 2 mg/kg/day and local prednisolone 10 mg/mL every 2 h). There was evidence of antitumor response in patient 2 consisting in a reduction in size and number of tumoral vitreous seeds which was evident after the first dose. Retinal tumors, however, remained unchanged in both patients after two doses. No significant changes in retinal function measured by ERG (photopic b-wave amplitude) were observed following VCN-01 treatment.

Histopathology studies of the enucleated eye from patient 1 showed a calcified and ossified tumor with areas of viable solid tumor, inflammatory exudates and extensive areas of necrosis. The tumor marker synaptophysin was positive in the viable tumor and in areas of tumor necrosis. Inflammation was confirmed by the presence of CD4 and CD8-positive T cells in the retina and necrotic tumor areas in the vitreous. Plasma cells (epithelial membrane antigen (EMA)-positive cells) were also abundant, likely explaining the high titer of anti-adenovirus antibodies in the vitreous at day 42 (1:2560). Areas of viable tumor contained a low number of T cells and plasma cells and were negative for the viral replication marker E1A. E1A and adenovirus 5 were identified in tumor necrotic areas, confirming VCN-01 replication and subsequent tumor lysis. No signs of necrosis or viral replication were observed in the conserved retina. Overall, our results suggest that the treatment was safe for the patient retinas and had anticancer efficacy.

After patients 1 and 2, whose data have been published, we included a third patient, at the dosage level 1/10 of the maximum feasible dose. This third patient saved his unique eye after responding well to treatment with VCN-01. We are analyzing the data and preparing the publication of this third case.

Question: Hi Doctor, if the optic nerve was enlarged in the MRI, what will be survival rate after intensive therapy?

Answer: These are patients that are more difficult to cure. Depending on the treatment given, survival is usually in the range of 30-50%. These patients need high dose treatment and orbital radiotherapy, it is important to be able to use techniques for identification of dissemination of these patients.

Question: What are the recruitment conditions for VCN01 clinical trials? How long is this therapy expected to be officially launched and will it be promoted globally?

Answer: Please check our WeChat official account, if you can read English, you can also check the hospital's official website, you can find links in the official account
The main recruitment criteria are: 1) patients have active retinoblastoma in one eye; 2) this active tumor is resistant or non-responsive after the use of all treatments available at the referral site; 3) enucleation is the only recommended treatment by the medical team treating the case at the referral site; 4) the patient is healthy regarding kidneys, liver, and bone marrow; and 5) the patient is older than one year old. So far, we are analyzing the data of the patients that have received the treatment.
Until we complete the clinical trial and analyze the results, we cannot anticipate whether VCN-01 will be promoted for global use. Thus, we cannot provide any estimation of the timings.

Question: Is your new treatment free

Answer: Virus Drug will be free, but secondary costs of the treatment will need to be charged, each case will do clinical evaluation and will receive our proposal with estimation...

Question: How much does it cost to get this treatment?

Answer: Each patient needs different treatment... the cost will really need to depend on the clinical evaluation...and what are the most appropriate treatments for the child