

## Endoresection of choroidal melanoma

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### Abstract

**Aims**—The results of 52 endoresections for choroidal melanoma are reported.

**Methods**—The current technique involves vitrectomy, retinal incision over or peripheral to the tumour, haemostasis by raising intraocular pressure and by moderate hypotensive anaesthesia, choroidal incision around tumour, endoresection with vitrector, endodiathermy to bleeding points and residual tumour, fluid-air exchange to reattach retina, endolaser to achieve retinal adhesion around the coloboma and destroy residual tumour in the sclera, silicone oil injection with removal after 12 weeks, cryotherapy to the sclerotomy, and adjunctive ruthenium plaque radiotherapy in selected cases.

**Results**—Patients receiving primary endoresection had a mean age of 53 years, a mean largest basal tumour diameter of 8.2 mm, and a mean tumour thickness of 3.9 mm. 40 tumours extended to within 2 disc diameters of the optic disc, with 17 involving disc. Follow up ranged from 40 days to 7 years (median 20 months). At the last visit, 90% of eyes were retained, with vision of 6/6–6/12 (two), 6/18–6/36 (three), 6/60 to counting fingers (18), hand movements (nine), and light perception (four). The main complications were retinal detachment in 16 and cataract in 25. Secondary endoresection (11) was performed after plaque radiotherapy (four), photocoagulation (four), trans-scleral local resection (two), and proton beam radiotherapy (one), with retention of the eye in nine cases. By the close of the study, no patients developed definite local tumour recurrence but one died of metastatic disease 41 months postoperatively.

**Conclusion**—Depending on tumour location, endoresection may conserve central vision or temporal field when radiotherapy would be expected to cause optic neuropathy. Longer follow up is necessary to establish the efficacy of tumour control. (*Br J Ophthalmol* 1998;82:213–218)

There is no ideal method for conserving vision in eyes with juxtapapillary choroidal melanoma. Plaque radiotherapy tends to cause radiational optic neuropathy<sup>1</sup> and there is also an increased risk of local tumour recurrence,<sup>2</sup>

because proper positioning of the plaque is prevented by the optic nerve. With proton beam radiotherapy of juxtapapillary tumours local tumour recurrence is less likely,<sup>3</sup> but there is still a high risk of radiational optic neuropathy.<sup>4</sup> With low energy, long duration laser photocoagulation, and indeed with any other form of photocoagulation, there is uncertainty as to whether or not the deeper parts of the tumour have been destroyed.<sup>5</sup> In addition, aggressive disc and choroidal neovascularisation, vitreous haemorrhage, and even rubeosis iridis can occur after closure of the major retinal vessels by the photocoagulation. Transpupillary thermotherapy with adjunctive plaque radiotherapy has been developed for juxtapapillary tumours.<sup>6,7</sup> Although early results are encouraging, it is still too soon to determine whether this treatment will avoid optic neuropathy and neovascular complications. Large choroidal melanomas, even those extending as far posteriorly as the fovea, can be treated by trans-scleral local resection,<sup>8</sup> but small tumours are more difficult to treat in this manner because they are more inaccessible and because they tend to separate from sclera so that they cannot be manipulated easily.

In 1989, one of the authors (BED) treated a patient with low energy, long duration laser photocoagulation, but there remained afterwards an excessive amount of residual pigmented tissue of uncertain viability. This was removed with a vitrector, both for diagnostic and therapeutic reasons. As there were no complications, it seemed reasonable to treat other juxtapapillary tumours with a similar procedure, which he named “endoresection”. Peyman independently developed similar techniques, which he called “internal eyewall resection”<sup>9</sup> or “retinochoroidectomy ab interno”.<sup>10</sup>

In this report, the early results of endoresection of small, choroidal melanomas are presented, and the surgical techniques are discussed.

### Materials and methods

Between March 1989 and August 1996, 52 patients with choroidal melanoma underwent endoresection, which was performed by the same surgeon (BD). This operation was performed either as a primary procedure (41) or as a salvage procedure, for suspected or definite tumour recurrence after other forms of treatment (11). Three patients receiving

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primary endoresection had been observed for tumour growth before surgery.

Patients were considered for endoresection if radiotherapy was considered to have a high risk of causing severe visual loss, either because of the proximity of the tumour to the optic disc (that is, less than 1 disc diameter), or because of previous radiotherapy. One patient, whose tumour involved the temporal part of the macula had endoresection in an attempt to preserve central vision in her only useful eye. In the latter parts of the study, patients were not selected for endoresection if the basal tumour diameter exceeded 10 mm or if more than a third of the optic disc margin was involved.

Patients were fully informed of all relevant aspects of the procedure, including the unusual nature of the treatment. From early 1993 onwards, all patients were given an audiocassette tape recording of their initial consultation to help them remember all information given to them.

Preoperative investigations included best corrected Snellen visual acuity, full ophthalmic examination of both eyes, B-scan ultrasonographic measurements of tumour dimensions, fundus photography, full blood count, and serum biochemistry with liver function tests. In three patients, ultrasonographic data were not available so that the tumour diameter was estimated from the fundus diagrams, assuming a disc diameter of 1.5 mm.

The technique of endoresection has changed gradually since it was first performed. Currently, the procedure begins with complete three port vitrectomy, with forced separation of the posterior vitreous and trimming of the vitreous base. A retinal incision is made in line with the nerve fibre bundle orientation with circumferential extension peripheral to the tumour to create a retinal flap. If, however, the tumour has invaded the retina, a direct approach is used. The retina over the tumour is detached, if necessary, by injecting fluid through the retinotomy, using a soft tipped cannula. An incision is made in normal choroid around the tumour with vertically cutting scissors, if possible without damaging the overlying retina. Alternatively, choroidal vessels around the tumour are closed with diathermy. The ocular blood flow is reduced to a level at which the disc vessels are closed or almost closed, by lowering the systolic blood pressure to approximately 50–60 mm Hg and if necessary by raising the infusion pressure. Before removing any instruments from the eye, the infusion pressure is lowered to avoid excessive retinal traction and tear formation near the sclerotomies. The tumour and surrounding normal choroid are removed piecemeal with the vitrector, leaving an area of bare sclera. Fibrotic tumour tissue (for example, after previous plaque radiotherapy) is first cut into thin strips with scissors to facilitate removal with the vitrector. After tumour removal, the infusion pressure is lowered until bleeding commences, so that all bleeding points can be recognised and treated by endodiathermy. The peripheral retina is examined, with indentation, so that if any entry site tears are found the

overlying vitreous is removed and cryotherapy applied. Next, fluid-air exchange is performed so that all subretinal fluid drains into the choroidal coloboma, from where it is aspirated with a flute needle. After several minutes, once the retina has flattened, a double row of confluent endolaser burns is applied around the coloboma to create retinal adhesion. In addition, the entire bed of the coloboma and the margins of the choroid are treated with strong laser burns, to destroy any residual tumour cells. The eye is filled with silicone oil, which is removed after approximately 12 weeks. Cryotherapy is applied to the sclerotomies to destroy any tumour cells that may have seeded to these areas. If the tumour has indistinct margins or extends far peripherally, a 15 mm or 20 mm ruthenium plaque is sutured to the sclera to cover as much of the coloboma as possible, without extending less than 1–2 mm from the optic nerve. The plaque is removed after a dose of approximately 100 Gy has been delivered to a depth of 3 mm.

Procedures that were attempted and then abandoned during the study include prior photocoagulation to the tumour and adjacent retina, and tumour removal under gas instead of fluid. Avulsion of the posterior vitreous and removal of vitreous near entry sites were not performed until late in the study. In almost all patients, the retinotomy was made directly over the tumour, but now a retinal flap is preferred.

The vitrectomy specimens were sent to the pathologist either fresh or mixed with formalin and were examined by cytology, histology, or both, after centrifugation.

Postoperatively, the patients were discharged from hospital after 2 days and then reviewed after approximately 1 week, 1 month, 12 weeks, then 6 monthly for 6 years, and eventually once a year, indefinitely. Follow up assessments alternated between the referring hospital and the ocular oncology service for about 2 years, when the patient was discharged back to the referring ophthalmologist. In the present study, follow up information on patients discharged from the ocular oncology service was obtained by requesting photocopies of the relevant pages of the case notes from the referring hospitals. The study was closed in September 1996.

Postoperative vision was measured with spectacles or pinhole. If there was a central scotoma after treatment of a macular tumour, then patients attending the ocular oncology service were tested for counting fingers vision in the temporal field. In other hospitals, vision may not have been tested eccentrically so that in such cases only a central vision of hand movements was recorded.

## Results

### PRIMARY ENDORESECTION

The 41 patients (17 male, 24 female) had a mean age of 53 years (range 21–87, SD 14.2). Concurrent diseases included diabetes mellitus (two), hypertension (one), ischaemic heart disease (one), hyperthyroidism (one), asthma (one), treated breast carcinoma (one), retinitis pigmentosa (one), and low tension glaucoma

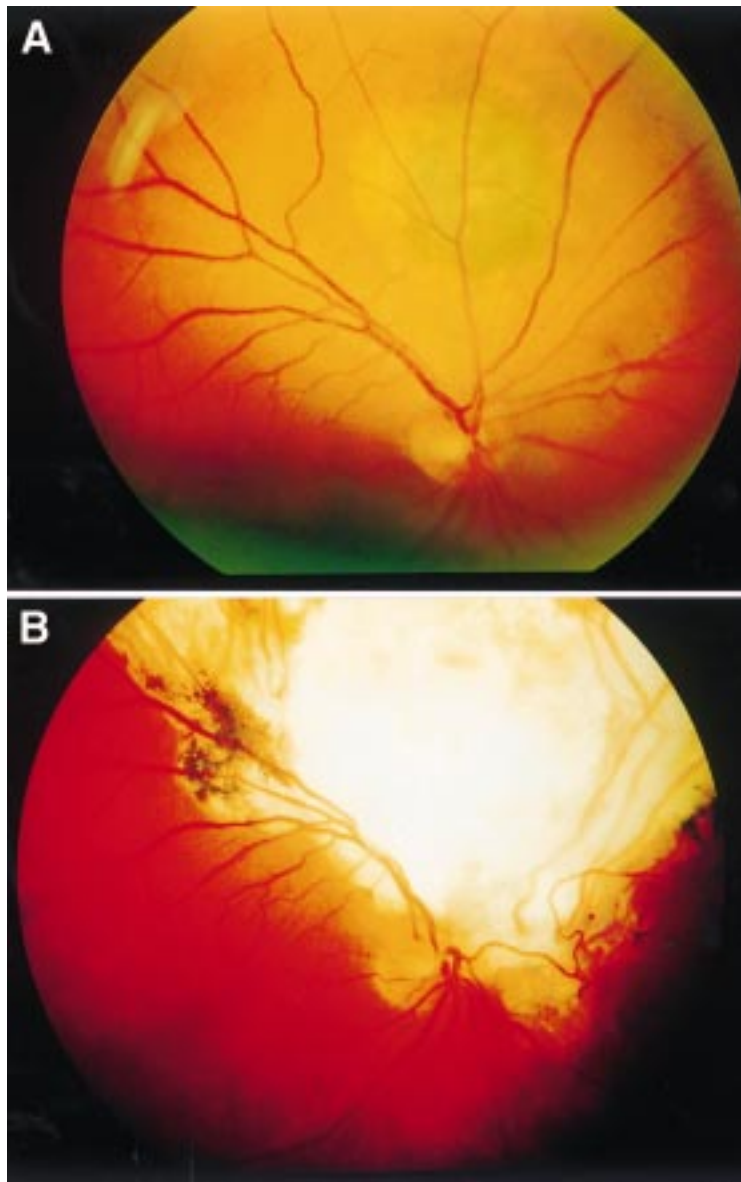


Figure 1 Right fundus of a 37 year old female, (A) preoperatively, showing a superior choroidal melanoma having basal dimensions of 4.6 mm by 4.2 mm, with a thickness of 2.3 mm, and (B) 22 months postoperatively, when the vision was 6/9. Histology showed the melanoma to be of mixed cell type.

(one). The tumour was located in the left eye in 21 patients and in the right eye in 20 patients. The preoperative visual acuity was 6/6–6/12 (23), 6/18–6/36 (eight), 6/60 to counting fingers (nine), and hand movements (one). The mean largest basal tumour diameter ( $n = 41$ ) was 8.2 mm (range 4.0–14.0, SD 2.4) and the mean tumour thickness ( $n = 39$ ) was 3.9 mm (1.5–10.1, 2.1). Except for one case, all tumours extended to within 2 disc diameters of the optic disc or fovea, with 10 involving fovea and 17 involving optic disc margin. The tumours extending to optic disc involved 1 (five), 2 (three), 3 (three), 4 (five), or 6 (one) clock hours of disc margin. The anterior tumour margin was pre-equatorial in three patients.

Histological data were available for 40 tumours, which were of spindle cell type in 18 cases and which contained epithelioid cells in

22. Histological evidence of malignancy was unequivocal in all but two cases, in which differentiation between naevus and spindle cell melanoma was uncertain. Both of these two lesions were observed to grow before treatment.

The follow up time to the close of the study varied from 40 days to 7 years, with a median of 20 months and a mean of 23 months.

At the final visit, 37/41 (90%) patients still retained the eye. Information on visual acuity is available on 36/37 patients and in these cases the vision was 6/6–6/12 (two), 6/18–6/36 (three), 6/60–counting fingers (18), and hand movements (nine), and light perception (four) (Fig 1). The reasons for enucleation were scleral perforation during endoresection (one), intractable retinal detachment (one), phthisis (one), and endophthalmitis (one).

The main intraoperative complications were inadvertent retinal touch at the macula (one), lens touch (one), inability to flatten detached retina (one), subretinal oil (one), subchoroidal oil (one), and scleral perforation while attempting to remove scleral fragments of tumour (one).

The main postoperative complications were retinal detachment (16), cataract (25), ocular hypertension (14), phthisis (one), epiretinal membrane (one), vitreous haemorrhage (two), possible local tumour recurrence (eight), and endophthalmitis (one).

The causes of the retinal detachment were subretinal injection of silicone oil (one), inability to flatten retina during endoresection (one), tear in atrophic retina due to contraction of laser scars (one), retinal tear during removal of subchoroidal oil (one), inadequate retinopexy around coloboma (one), vitreous traction at the margin of the coloboma (one), entry site tears (seven), retinal break in degenerative retina (one), and uncertain (two). The time between endoresection and diagnosis of retinal detachment averaged 100 days (range 0–367, SD 102). Retinal detachment surgery was performed in 13 cases, either by a vitreoretinal surgeon at St Paul's Eye Unit (12) or at the referring hospital (one) and was successful in 11 patients, after one (four), two (four), three (two), or four (one) procedures.

Cataract occurred in 25 patients, mostly as a consequence of the use of silicone oil. Eleven patients had elective lens extraction. Another six patients had lensectomy as part of a vitreoretinal procedure for retinal detachment, and one had lensectomy during endoresection because of lens touch.

Fifteen patients developed acute ocular hypertension, which occurred at an average of 13 (range 1–61) days after the endoresection. In these patients, the intraocular pressure rose to a mean of 40 (range 27–74) mm Hg. The pressure was controlled medically in almost all patients, in whom it was usually possible to discontinue treatment after a few days. In one patient, the pressure remained high until the oil was removed.

Phthisis occurred in one patient, who was a 67 year old man with an initial tumour diameter of 11 mm. This eye was enucleated at

the referring hospital when cataract prevented adequate examination of the posterior pole.

One patient, a 60 year old female insulin dependent diabetic, developed endophthalmitis immediately after the endoresection and had the eye removed when the prospects for recovering vision were poor.

There were seven patients who had laser photocoagulation applied to areas of increased pigmentation at the margins of the coloboma because differentiation between reactive pigment epithelial hyperplasia and tumour could not be made. One patient had a suspected recurrence, which on biopsy proved to be suprachoroidal silicone. Another patient was referred back to the ocular oncology service with a suspected tumour recurrence, but the tumour was shown by magnetic resonance imaging to be a bubble of suprachoroidal silicone.

In the enucleated eyes, microscopic deposits of residual tumour were found in two cases, and these were located at the margin of the coloboma in both cases.

One patient, a 33 year old man, died of metastatic disease after the close of the study, 41 months after endoresection of a 14 mm diameter melanoma of mixed cell type. One patient died of a cerebrovascular accident and another as a result of gastrointestinal disease.

#### SECONDARY ENDORESECTION

The 11 patients (six male, five female) had a mean age of 51.7 years (range 28–72, SD 14.2) at the time of the endoresection. The initial treatments in the patients receiving secondary endoresection were trans-scleral local resection (two), ruthenium plaque radiotherapy (four), proton beam radiotherapy (one), and laser photocoagulation (four). The time between the primary treatment and endoresection ranged from 4 to 86 months, with a mean of 27.8 months (SD 26.1). The follow up times varied from 4.2 to 80.7 months (median 35.8; mean 40.0; SD 23.6).

Nine patients retained the eye by the close of the study with the vision at the final visit being recorded as 6/18–6/36 (two), 6/60 to counting fingers (six), and hand movements (one). Several patients had macular dysfunction as a result of the primary treatment. Complications occurring as a result of the endoresection included cataract (three), macular damage by choroidal neovascular membrane from the surgical coloboma (one), retinal detachment (one), and pseudo recurrence of intraocular tumour (one).

Two patients eventually had the eye enucleated. One of these patients was a 33 year old woman who had endoresection after unsuccessful laser photocoagulation elsewhere. Seven months after the resection, she was noted to have diffuse pigmentation at the margins of the coloboma, which was suspected as local tumour recurrence. Histologically, this pigmentation proved to be an accumulation of melanomacrophages. The other patient, a 52 year old man, had endoresection when laser photocoagulation failed to destroy two juxtapapillary local recurrences in a surgical colo-

boma after trans-scleral local resection. After the endoresection, he developed a localised inferior retinal detachment, which remained stable, but the eye was enucleated by the referring ophthalmologist when he developed a dense cataract. Histological examination showed microscopic deposits of residual tumour in the surgical coloboma.

All patients having secondary endoresection were alive at the close of the study, with none having recognised metastatic disease.

#### Discussion

The endoresection techniques used in this series have changed over the years. Initially, the technique was used as a salvage operation, to remove bulky residual pigmented tissue after low energy, long duration laser photocoagulation.<sup>5</sup> In subsequent cases, laser retinopexy was performed about a month before the endoresection, but this was abandoned because adequate retinal adhesion could not be achieved if there was any significant amount of exudative retinal detachment and because in at least one case the tumour was found to extend beyond the ring of laser scars. Intraoperative retinopexy was therefore preferred, with the laser photocoagulation performed after removal of the tumour. In the initial stages, detached retina could not be reattached during the endoresection, and Peyman has reported similar difficulties.<sup>9</sup> In the present study, this problem was eventually solved by performing fluid-air exchange so that all subretinal fluid drained into the choroidal coloboma, from where it was aspirated with a flute needle. At first, only gas tamponade was used after endoresection, but severe vitreous haemorrhage occurred, which stimulated the use of silicone oil. Another problem occurring in the early stages of this study was the development of tractional vitreous bands extending to the margins of the coloboma, but these are now prevented by inducing posterior vitreous detachment at the start of each endoresection procedure. For most of the study, only a limited vitrectomy was performed near the vitreous base, so as not to damage lens, but now a more extensive vitrectomy is carried out, using indentation, so as to prevent entry site retinal tears. In some patients, trans-scleral cryotherapy was applied to the tumour immediately before removal, but this was abandoned because optic nerve damage occurred despite taking precautions. Because of the way in which the procedure has evolved, the results reported in the present paper do not reflect the current potential of the procedure.

The results reported in this study are broadly similar to those of Lee *et al*, who described their results with 23 patients.<sup>10</sup> In their series, which included seven non-melanomas, 10 patients retained vision of 20/400 or better, three patients died of metastatic disease, two patients subsequently had enucleation, and one had local tumour recurrence. As in the present study, several patients developed transient ocular hypertension in the immediate postoperative period, and a few also developed cataract. Unlike the

present study, only one patient developed postoperative retinal detachment. It is difficult to compare results from different centres, however, as there are likely to be differences in case selection as well as in the categorisation of preoperative characteristics and postoperative outcomes. It is hoped that future studies with larger numbers of patients will allow risk factors for various outcomes to be defined statistically so that results can be reported more meaningfully.

Follow up times are too short for comment on local tumour control and metastasis, and it is inevitable that these complications will eventually occur in some patients, as is the case with any other form of conservative treatment. On theoretical grounds, the tumour might recur (1) in the uvea at the margins of the coloboma, as a result of incomplete excision, (2) in the orbit, because of inadequate photocoagulation and diathermy to the sclera, (3) in other parts of the eye, owing to seeding at the time of the operation, and (4) systemically, owing to tumour dissemination at the time of the resection or postoperatively, from residual tumour. Measures currently taken to minimise these risks include (1) making choroidal incisions around the tumour before manipulating it, to prevent tumour dissemination into the general circulation, (2) closure of the choroidal circulation during endoresection by reducing the systemic blood pressure and increasing the intraocular pressure, as an added precaution against intraoperative metastasis, (3) wide excision margins and photocoagulation to the adjacent choroid, to prevent marginal recurrences, (4) endodiathermy and photocoagulation to the bed of the coloboma, to destroy any residual intrascleral disease, (5) cauterisation of instruments before removal from the eye and cryotherapy to the sclerotomies, to prevent tumour seeding to entry sites, (6) adjunctive plaque radiotherapy if tumour removal is uncertain, and (7) postoperative monitoring, to identify and treat any recurrences without delay so as to reduce the risk of tumour spread from such recurrences. Further possible measures, which have yet to be evaluated, include (1) diode laser treatment applied to the tumour immediately before endoresection, and (2) destruction of any intrascleral tumour immediately after endoresection either by plaque or radiotherapy or by application of diode laser photocoagulation both to the inner scleral surface, using an endolaser probe, and to the outer scleral surface, using a right angled probe.

The creation of a circular retinotomy over the site of the choroidal tumour gives good access to the tumour, especially if the tumour extends close to optic disc, but a large retinal opening causes peripheral visual field loss and may increase the chances of proliferative vitreoretinopathy and ocular hypotension. Peyman *et al* have removed choroidal tumours from under retinal flaps<sup>11</sup> and other workers prepare extensive retinal flaps for the removal of subretinal haemorrhage, but they report a high rate of retinal redetachment after such extensive surgery (K Lucke and S Bopp, personal communication, XXth Meeting of the Club

Jules Gonin, Bern, September 1996). Although a retinotomy directly over the tumour is well tolerated, we have recently started preparing a retinal flap in the hope that there might be better preservation of vision.

The most serious complication has been retinal detachment. Initially, this was due to vitreous bands pulling on the margins on the coloboma, but this problem was eliminated by performing an adequate vitrectomy including removal of posterior cortical vitreous. As mentioned above, retinal detachment during the endoresection was successfully treated by performing retinopexy under gas. Throughout this study, retinal detachment from entry site tears was a persistent problem. This seems to have been remedied by (1) trimming vitreous base near entry sites, (2) avoiding a high infusion pressure when removing instruments, (3) examining the peripheral retina for breaks, using indentation, and (4) applying cryotherapy and/or endolaser photocoagulation if any tears are present. Further studies are necessary to evaluate the efficacy of these measures.

It is perhaps too soon to define the indications for primary endoresection. This procedure should be reserved only for eyes that are not expected to do well after more conventional forms of treatment—that is, (1) small tumours extending to within 1 disc diameter of the optic disc, and (2) growing tumours previously treated by radiotherapy. It would be difficult to justify endoresection for tumours than can satisfactorily be treated by more conventional methods, such as plaque radiotherapy, proton beam radiotherapy, and even trans-scleral local resection. For equivocal cases, it would be ideal if different treatments could be compared by randomised prospective studies, but such studies are logistically difficult to perform because few centres provide proton beam radiotherapy and suitable tumours are rare at any one centre.

The histological studies performed on the endoresection specimens were interesting. We were surprised that apparently growing tumours after plaque radiotherapy usually consisted of melanomacrophages and fibrous tissue with no definite evidence of viable tumour tissue. Another unexpected finding was the presence of epithelioid cells in so many small melanomas, including a case with a tumour thickness of less than 2 mm. After trans-scleral cryotherapy of small tumours, we were impressed by the finding that most of the tumour tissue was necrotic (P Hiscott, PA Smith, BE Damato, unpublished data).

In conclusion, endoresection of uveal melanoma may conserve the eye and vision when other forms of conservative treatment are likely to cause severe ocular complications. The main problem following endoresection is retinal detachment which, unlike radiational optic neuropathy, is preventable and usually treatable. Further studies are required to establish the efficacy of endoresection with regard to local tumour control and metastatic disease.

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