EUROPEAN HUNTINGTON'S DISEASE NETWORK

Advancing Research, Conducting Trials, Improving Care

EHDN Platform Meeting

uniQure Topline Results: Unpacking the Outcomes so Far

in collaboration with the Huntington's Disease Youth Organization

and European Huntington Association

Full recording available on the EHDN YouTube channel:
https://www.youtube.com/watch?v=wKj1JRfJBRE

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EHDN Executive Committee Chairs **Patrick Weydt** (University of Bonn) and **Åsa Petersén** (Lund University) welcomed more than 380 delegates to the highly anticipated platform meeting held on 18 November 2025. Åsa chaired the scientific programme, which provided background, context, and the latest insights into the AMT-130 topline results, followed by a panel discussion and a question-and-answer session.

Scientific Presentations

Anne Rosser of Cardiff University, a former EHDN chair and investigator on the AMT-130 trial, opened the scientific presentations by providing background to the research. She explained that AMT-130 is a gene therapy – a tiny piece of DNA that codes for a microRNA. The approach lowers both mutant and wild-type huntingtin, and importantly, lowers the highly toxic exon 1 fragment as well as the full-length huntingtin protein. The idea is that the DNA remains in the brain cells (neurons) long-term, functioning as a miniature factory that continuously produces microRNA. This would potentially allow a single treatment of AMT-130 to durably reduce huntingtin levels.

To effectively deliver AMT-130 to its target in the brain, it is packaged into a viral vector – a modified AAV5 virus that carries the DNA and has a predilection for entering neurons rather than other cells. The virus is modified so it can no longer replicate, and the viral capsule is eventually cleared from the neurons, leaving only the DNA, which persists. Because viral particles cannot cross the blood-brain barrier, they must be delivered directly via a stereotactic neurosurgical procedure.

This highly controlled procedure was conducted at a small number of sites in the USA and Europe (Cardiff, UK, and Warsaw, Poland). The procedure is performed in an MRI scanner using an MRI-compatible stereotactic delivery frame, allowing the infusion to be closely monitored. The ClearPoint Convection Enhanced Delivery system means that the gene therapy can be placed to fill the volume of the striatum with a 2 cm caudate volume cut-off. It is anticipated that retrograde transport from medium spiny neurons also distributes some of the therapeutic to the cortex.

This is pioneering neurosurgery, and given the relatively early stage of clinical development, the operations take considerable time – around 14 to 18 hours. However, discussions are ongoing to consider how to reduce the surgical duration. For example, the EHDN Neurosurgical Taskforce, under the leadership of William (Liam) Gray (Cardiff University) and Romina Aron Badin (MIRCen), has been working over recent years to address challenges in the neurosurgical delivery of gene and cell therapies. In September, an in-person workshop of the EHDN Advanced Therapies Working Group in Venice brought together neurosurgeons and neuroscientists from across the USA and Europe to discuss how to address these challenges. It is hoped that the duration of surgery can be substantially reduced, and that it may even be possible in the future to perform it in a day case setting.

The AMT-130 research represents an ongoing series of studies, some of which can now be reported jointly. The first two studies were low-dose and high-dose versus placebo studies conducted in the USA. The high dose is approximately 10 times the potency of the low dose. A similar study was conducted in Europe without a placebo arm (as European regulators did not approve it). The placebo surgery was a parietal burr hole in the skull, and patients were kept under anaesthesia for an equivalent duration as in the treatment arm. After 12 months, participants in the placebo arm were offered treatment; four were eligible and accepted the offer.

Patients were randomised to high- or low-dose AMT-130. Ongoing studies are testing the use of immunosuppression to reduce the risk of adverse reactions to the viral capsid (a protective protein shell that encases the genetic material) and to assess whether AMT-130 can be safely delivered to participants with a lower caudate volume.

The currently available data are from participants in the USA and European studies who completed 3 years of follow-up. This includes data from 12 participants in the low-dose group and 12 in the high-dose group, whose results were compared to propensity-matched patients from Enroll-HD. This

approach was prespecified and agreed in advance with the FDA. The primary endpoint was the composite Unified Huntington's Disease Rating Scale (cUHDRS™), and secondary endpoints were Total Functional Capacity (TFC), Symbol Digit Modalities Test (SDMT), Stroop Word Reading Test (SWR), and Total Motor Score (TMS) change from baseline at 36 months. The supporting endpoint was cerebral spinal fluid (CSF) neurofilament light chain (NfL) change from baseline at 36 months.

Sarah Tabrizi of University College London, an investigator on the AMT-130 trial, presented the topline results from cohorts 1 and 2 at 36 months, which included data from the low- and high-dose groups. She opened by explaining that the clinical measures used in the AMT-130 studies enable objective measurement of disease progression with validated tools. More specifically, the cUHDRS™ captures multiple domains of HD, including motor, cognitive, and functional abilities. The TFC specifically measures decline in functional capacity, such as the ability to work, manage finances, and maintain self-care. In both scales, scores typically decrease over time, reflecting worsening in motor, cognitive, and functional domains. This decline is closely linked to loss of independence and daily living skills.

The external comparator (control) data were primarily from Enroll-HD, an ongoing longitudinal observational study conducted to rigorous standards. The prespecified pivotal analysis of treatment data versus natural history control data was aligned with, submitted to, and approved by the FDA in advance of database lock.

In clinical trials, it is necessary to compare two groups: participants who receive the experimental treatment and those who do not (control group). In a randomised controlled trial, participants are randomly assigned to groups, helping ensure comparability across groups in terms of age, health status, and other characteristics. Sometimes, however, this randomisation is not possible, particularly in the case of invasive gene therapies with very small numbers of participants and follow-up periods spanning several years.

Propensity score matching is a statistical approach used in the study of rare diseases where it may be difficult to have a placebo group. Already, several gene and advanced therapies have been approved in the USA and Europe using propensity-score-matched external comparator groups. The approach aims to mimic the randomisation process by making the two groups as similar as possible in terms of their characteristics.

Consideration of the baseline demographics between the AMT-130 high-dose group and the propensity-score-matched external comparator group showed that the groups were well matched for age and fairly well matched for gender. In terms of baseline clinical characteristics, the standardised CAG-Age product (CAP100) score and Diagnostic Confidence Level (DCL) were very well matched, as were TFC, SDMT, SWR, and TMS.

The study met its cUHDRS™ primary endpoint at 36 months. For the 12 participants who received the high-dose, the deterioration over 36 months was 0.38 – statistically significantly lower than in the external comparator group. This represents a 75% slowing of disease progression as assessed by the cUHDRS™. Looking at the data at 12, 24, and 36 months, the separation between the treatment and external comparator groups is apparent by 24 months and even more clearly evident at 36 months.

A key secondary endpoint, TFC, showed a 60% reduction in the AMT-130 high-dose group compared with the external comparator group at 36 months. Note that the 2025 paper by Marcelo Boareto and colleagues analysing placebo data in GENERATION HD1 showed that TFC is strongly resistant to placebo effects even after 24 months. The paper also showed that TMS placebo effects are washed out by 17 months, and by two years, placebo effects on the cUHDRS™ and cognitive measures are washed out.

In terms of clinically meaningful worsening, the high dose reduced the odds by more than 60% (68% on cUHDRS™ and 62% on TFC) compared with the external comparator group at 36 months. For the other secondary endpoints, supportive trends for disease slowing were observed with the high dose across all clinical subdomains of the cUHDRS™, including 88% reduction for SDMT, 113% reduction for SWR, and 59% reduction for TMS. For the low dose, variable trends were observed across the functional, motor, and cognitive endpoints, potentially suggesting a dose-dependent effect, with the clearest benefit at the high dose.

An important exploratory, supportive endpoint was CSF NfL, which, as a marker of neural degeneration and injury, increases with HD progression. Filipe Rodrigues and colleagues showed in 2020 that in early symptomatic patients (as recruited in the AMT-130 studies), CSF NfL typically increases by approximately 10% each year. In the AMT-130 studies, CSF NfL was below baseline at 24 and 30 months, and at 36 months it was 8.2% below baseline for the high dose and 4.7% below baseline for the low dose. This suggests that at the high dose at 36 months, CSF NfL was reduced by 30–40% relative to expected levels.

Adverse events were mainly related to the surgery or the lumbar punctures required to assess CSF, meaning that both doses of AMT-130 were generally well tolerated and presented a manageable safety profile. The majority of drug-related serious adverse events occurred within the first few weeks post-treatment and were fully resolved with steroids or symptomatic treatment. No drug-related serious adverse events occurred after December 2022.

In summary, high-dose AMT-130 met its primary endpoint and a key secondary endpoint at 36 months, with favourable trends observed across additional clinical and supportive endpoints. Data suggest a slowing of disease progression on the cUHDRS™ and the TFC compared to an external comparator at 36 months. Favourable trends were observed across other clinical subdomains of the cUHDRS™ along with reductions from baseline for CSF NfL, a marker of neurodegeneration. AMT-130 is generally well-tolerated and has a manageable safety profile.

Panel Discussion

Sarah Tabrizi opened the panel discussion with her perspective that, for the first time, we have proof-of-concept data showing that HD can be modified in early symptomatic individuals. So far, we have seen that among the 12 individuals who received the high dose, the clinical progression of disease appeared significantly slower than expected based on natural history studies. This was supported by objective molecular evidence, i.e., CSF NfL, a marker of neurodegeneration. CSF NfL did not increase over time as would be expected based on natural history data. When CSF NfL levels decrease – as seen in the AMT-130 studies – it suggests that neurons are potentially being saved. Together with the molecular lowering of CSF NfL and objective clinical evidence, we have reason to believe that the high dose of AMT-130 may potentially modify and slow HD progression. In sum, the study met its primary endpoint and a key secondary endpoint, both of which were prespecified.

Nonetheless, there are several very important points to highlight. AMT-130 was tested in only a small number of patients and the study is ongoing. More participants will be dosed, and in due course, more data will be available. This is the nature of gene therapy – it is highly complex and involves small numbers of participants with long follow-up. Meanwhile, people are working hard on a scientific publication to present the existing data in full.

There has been a lot of discussion about the external comparator group, and although this is new for HD research, the approach is well recognised in other rare diseases by regulatory agencies. An external comparator group is a validated method for assessing highly invasive gene therapies. And although it is the best that we currently have for this sort of research, it is not perfect. It is very challenging to ask

people to undergo a complex neurosurgery with the possibility of being placed in a placebo group for three or four years, during which time their disease may progress. In the USA, the study had a placebo (sham surgery) arm, but it was approved by the ethics board only for the first 12 months. After this time, participants had the option to take up the treatment, consistent with current ethical principles and standard regulatory guidelines. Four participants received treatment (three at the high dose), but as of yet, the data are not particularly helpful when we want to look at three years of longitudinal data. Moving forward, as we develop more advanced therapies like gene therapy or cell replacement therapy in HD, we will be discussing external comparator groups more frequently.

Overall, the data suggest that lowering mutant huntingtin and all its toxic forms may help preserve neurons and, in turn, slow the decline in neurological function. The principal limitations are the small number of participants studied so far and the fact that, due to the nature of gene therapy, there is no three-year randomised placebo group, necessitating external comparator data.

The evidence that HD may be modified in early symptomatic patients is very exciting. Now we have to build on these results. This may be the beginning of the end – and if we do this together as a community united, we will be stronger.

Anne Rosser emphasised that while the current results are encouraging, the presentations confirm that we are still early in the development process. The continuation of the trial, further data emerging from participants already in the study, and, hopefully, more participants coming through and longer periods of follow-up, will be critical.

AMT 130 may have potential as a future therapy, but we need to confirm that the treatment really does work and that the results are persistent. Currently, the surgery itself is quite complex and is performed only in specialist centres – but it is very important that the existing surgery is not considered the only way such a treatment could ever be given. EHDN's Neurosurgical Working Group and the neurosurgeons involved in the study are optimistic that, in the future, more efficient ways of delivering AMT-130 are likely to be established. For example, it may be possible to implant indwelling cannulae under anaesthesia and then allow participants to be awake while the infusions take place. While this methodology would take some years to develop and refine, it should be recognised that the 14–18 hours of surgery required at this early stage is not necessarily the endpoint.

Whether AMT-130 becomes a viable therapy or not, other therapies remain firmly in the frame. This recent progress encourages us that lowering huntingtin as a general approach holds significant promise. Other treatment modalities are also very important, and we will need a variety of different ways to provide effective therapeutics for HD.

Dina De Sousa is an HD family member and a patient advocate. She is also a board member of the European Huntington Association and a patient representative on the EHDN Executive Committee. Dina explained that as an HD patient, she has followed uniQure, along with other pharmaceutical companies, for several years and watched things grow. When the topline results were announced, her reaction was one of excitement and the shared belief that this is a scientific breakthrough.

Dina noted that the surgery, as it currently stands, is very invasive, but that this is likely to change in the future, making it more readily available to other patients. She acknowledged that gene therapy remains a delicate and tricky subject, but remains hopeful that effective treatments for HD will be found for future generations, noting that a range of treatment options will be needed.

Dina concluded that while there has been significant disappointment for the HD community in recent years, the uniQure topline results represent a life-changing breakthrough. There is still a lot to do, and as a community, Dina suggests we need to be patient on the road ahead.

Jenna Heilman (Executive Director, Huntington's Disease Youth Organization) shared her view that the findings represent a key piece of the HD research puzzle. She argued for a balance between cautious optimism and realistic expectations, noting that even when a therapy is approved for HD, not everyone will be able to receive it – potentially due to location, treatment costs, disease progression, and many other factors.

As such, Jenna explained the need to remember that families are living with HD in a variety of different ways every single day. News such as the uniQure topline results inevitably raises a multitude of questions. Continued partnership among scientific partners, advocates, and the HD community is critical to help mitigate the multifaceted feelings and expectations and to provide support.

Jenna concluded by emphasising the continued role of partnership within the HD community, the need to educate the community on gene therapy and other research developments, and the necessity of improving access to regulatory conversations.

Ignacio Muñoz-Sanjuán (Chief Executive Officer and Chairman of the Board at Rumi Scientific; Founder and President of Factor-H Foundation) shared that uniQure's recent results have created significant confusion for the patient community, compounded by the mass media which portrayed AMT-130 as a curative or effective treatment, as if it would become available as an approved therapeutic. He noted that events such as this platform meeting can go a long way towards addressing that confusion and uniting the HD community.

Ignacio reiterated that we do not yet have all the information available from the trial, and he hopes that in time, uniQure will make it available. Meanwhile, he noted, we know the sample size was small, and there are professional criticisms suggesting the potential for placebo effects following invasive surgery to confound the interpretation of the trial results presented to date.

A key focus for the HD community should be on coming together to take on board this potentially transformative news. If the results continue with more participants over a longer period of time, the approach will be a giant step forward. Ignacio added that huntingtin-lowering therapies had not previously been delivered directly into the basal ganglia, and there was some scepticism that this could be achieved in symptomatic patients. It is a clear win for the field to confirm that delivering a gene therapy directly into the basal ganglia is possible and well-tolerated. Ignacio urged everyone in the HD community to come together, given the reasons for optimism – but also to be patient. He also argued for increased awareness of how the community at large responds when potentially positive news is delivered and the importance of continuing to work together.

Patrick Weydt provided concluding comments on the panel presentations, emphasising the importance of communication, particularly when dealing with incomplete knowledge and science, and the impact of such findings and the language used on those impacted by HD in their daily lives.

The platform meeting concluded with a question-and-answer session. Unfortunately, the speakers and panellists were unable to address all submitted questions due to limitations in the publicly available data and the time constraints of the meeting.

1. What is 'clinical meaningfulness'?

ST: Clinical meaningfulness is a measure that regulators use to assess whether a drug has a beneficial effect on things that matter for patients –such as how they think, feel, and how they are managing their lives. Cristina Sampaio, Chief Medical Officer at CHDI, was the lead author in a 2023 paper on clinically meaningful change in HD. The concept of minimal clinical difference was originally developed

to assess the relevance of drug-related improvements and later adapted to assess changes in deterioration. Humans have a lot of difficulty perceiving slow deterioration versus short-term improvement; therefore, the values found in minimal clinically important difference are typically very large. Because HD progresses very slowly, it is a crude measure of the value of an intervention. Ed Wilde at University College London has also recently published a commentary on clinical meaningfulness.

DDS: From a patient's perspective, clinically meaningful change means being able to manage finances for a few years longer, being able to go for walks longer, and being able to dance with grandchildren. All these little steps would add to the quality of life for someone with HD.

AR: In HD, we are aiming to slow rather than stop decline – which makes it quite difficult to measure. That said, in the uniQure results there was a quite clear slowing of decline. The longer one follows a slowing in decline, the more meaningful it becomes. There is no simple answer because when faced with having no therapy at all, even a slight slowing for a few years could mean a very big difference for an individual.

2. Would it be helpful to use a placebo group from another study for comparison?

ST: If there are three years of placebo data from another study, it would be wonderful for that to be made available for the community. Roche has already made the two-year placebo data from GENERATION HD1 available. Sharing data in the HD community is vital, not just for AMT-130 but for the development of other therapeutics.

3. What do we know about CSF mutant huntingtin levels?

ST: These data haven't been shown in recent presentations, and I am not sure why. However, I can comment on the assay. The CSF mutant huntingtin assay is technically challenging and has low sensitivity. Early in the disease course of HD, it cannot be measured, and there is only a very small amount of mutant huntingtin available in the CSF – much of it is tied up in neurons in the brain. This is compounded by the fact that the striatum is really quite a small structure. In preclinical studies, significant reductions in mutant huntingtin were observed in the striatum of pigs, but not in the CSF. So, for a gene therapy like this, we may not see changes in CSF mutant huntingtin. If we had the huntingtin PET ligand, it would be much easier. In any case, we know that while CSF mutant huntingtin is important, it is not a useful biomarker of HD progression and does not correlate with clinical improvement, as seen in GENERATION HD1.

4. What can you tell us about the imaging data?

ST: These data are not yet available but will be shared in a future medical publication. Those of us running the study could see the effects of the neurosurgical procedure on MRIs post-dosing, and I expect that the structures of the caudate and putamen will be affected in particular. We look forward to seeing the imaging data when published.

5. What is the regulatory situation?

PW: I cannot speak on behalf of the European Medicines Agency, but I do know they are very aware of the challenges researchers face when testing specific interventions in rare diseases. They are also aware that traditional placebo groups are not feasible for the reasons we have discussed today. There are clearly transitions and shifts underway at the FDA, but it is difficult to comment on this from

Europe. It is important for players such as EHDN to engage in dialogue with regulators, who are under significant pressure, including from those in the business of commercialising these interventions.

6. Has increased awareness of HD led to more people getting in touch with HD organisations?

JH: Absolutely. We were at the European Huntington Association conference in Bucharest when the uniQure news broke, and we were working around the clock trying to answer the questions coming in. People really want to understand how to get treatment for themselves or their loved ones.

I'm part of a group called the Cures Collective in the USA, and we're working collaboratively to raise awareness of the questions and the support needs of communities not only in HD but also in other neurodegenerative diseases. The news from uniQure really highlighted this need for collaboration.

DDS: This has really put HD on the map. The news from uniQure seemed to reach every news channel, which is fantastic for raising awareness. But it also raises the need for balance – we saw reports of a 'cure' for HD, which is incorrect. Many people contacted the European Huntington Association and other organisations to find out where they could sign up for the treatment. Clearly, there are lessons to be learned about how to engage with communities and how to deliver such news in the future.

IM-S: In Latin America, like in Europe and in the USA, those of us working in the field received a lot of questions from the HD community – from patients and professionals –wanting to understand the meaning of the results, having seen the news. My main reflection would be to emphasise the need for a direct communication strategy among pharmaceutical companies, organisations such as EHDN and the Huntington Study Group (which enabled the trials to happen in the first place), and patient organisations. This would allow us, as a community, to be better prepared to answer questions that affect the daily lives of people impacted by HD and to avoid unnecessary confusion and angst. Collectively, we should reflect on how we could manage this better in the future.

7. How can people get involved in this or similar trials?

AR: The uniQure trial is not recruiting in Europe at the moment, but we very much hope that there will be opportunities for participants to join this research in the future. There are a lot of clinical trials that are currently open and others in the pipeline, so potential participants should think carefully about these opportunities and talk to their physicians for advice. The best way to get involved in clinical research is to join the Enroll-HD study. In many centres, patients are recruited from Enroll-HD into interventional trials, so it's a great place to start.

8. Do the uniQure results change anything about presymptomatic genetic testing?

ST: No, these results do not mean that people should rush out to get predictive genetic testing unless they were already planning to do so. Predictive genetic testing is a very personal decision, and if someone had no prior plans to undertake it, these results should not change that. These are early results and an important step forward, but we don't yet have a regulatory-approved treatment for HD. If we get to that point in the future – and we're all working very hard towards that –that may change people's uptake of predictive genetic testing.

9. If the virus used to administer AMT-130 doesn't replicate and spread, how does it reach other parts of the brain?

AR: We know that neurons connect with other neurons in the brain, and viruses may be transported along axons and dendrites and can cross into other neurons. This has been observed in large animal studies, but at this stage, it is not entirely clear to what extent this is the case in humans.

10. How long does the microRNA stay in the brain?

AR: As far as we know, the DNA persists indefinitely in the brain, and as DNA codes for microRNA, it keeps on producing it. In the data we have, the DNA appears to have retained activity over three years in the participants who have been followed up. One would hope and expect that it will continue to be expressed and remain active, but this has yet to be confirmed with data from longer-term follow-up.

IM-S: The distribution of the virus has been fairly well-studied both in primates and in the transgenic 'minipig' model of HD, and this understanding was critical to the decision to move the AMT-130 programme forward. The distribution of AMT-130 through the axonal terminals from the thalamus and deep layer cortical neurons, as well as through projections from the globus pallidus and substantia nigra, means that the compound is not just targeting the striatum. If AMT-130 behaves the same way in humans as it does in monkeys and pigs, it is reaching almost every major structure of the basal ganglia and connected areas. This may be very significant for understanding the differences between the effects of the high versus the low dose, which would affect the extent of distribution.

In the minipig model of HD, a significant effect on CSF mutant huntingtin was observed – a decrease of about 20%. This was much lower than the deeper parenchymal (brain tissue) lowering of huntingtin. So, the expectation was that AMT-130 effects on CSF mutant huntingtin in humans would be much smaller than observed for antisense oligonucleotide therapies. For this reason, it is not surprising that these data haven't been presented yet, but it is important to see these findings in due course. There are many unanswered questions, but we know from gene therapies for other disorders, such as Parkinson's disease, that AMT-130 has the potential to be a very long-lasting therapeutic. In the Ceregene AAV-neurturin gene therapy study, for example, post-mortem analysis showed transgene expression 10+ years after the initial surgical procedure.

11. What can researchers in other rare disease fields learn from these developments so far?

PW: HD is a paradigmatic monogenic disease, and certainly, researchers in other fields are closely watching these developments. From both the scientific and regulatory perspectives, other fields look at HD because we are in the unique position of being very large within the rare disease field and also well-organised. We can hope that advances in dialogue with regulators will also benefit other disease groups.

DDS: Just as we learn from other disease fields, other fields learn from us through cross-sectional procedures. Gene therapy is a very complex procedure, and there is much to learn and share across different fields.

JH: Advocacy is a clear component in which we can all lean on each other in rare diseases, especially in HD. Nobody will develop HD unless they come from a family that carries the gene, so the advocacy effort from outside the community is much more limited. But for Parkinson's disease and multiple sclerosis, for example, awareness generally is much higher, and we have some common things to work towards. These include obtaining natural history data and coming together to discuss advocacy points on accelerated approval, openness, and communication. We have a big opportunity for different advocacy organisations to work together, even across different disease areas.

12. What is the potential for selection bias due to the required minimal striatal volume in the AMT-130 research? Did propensity matching take striatal volume into account?

ST: The original propensity score matching was based on clinical characteristics but was also conducted using the TRACK-HD and PREDICT-HD datasets. When the cohorts were matched for striatal volume, this did not affect the results. These data were presented at the 2025 HD Clinical Research Congress and will be included in the publication. TRACK-HD and PREDICT-HD are historical datasets, whereas regulators prefer concurrent datasets conducted as clinical trials, such as Enroll-HD. But as there are no imaging data in Enroll-HD, historical datasets had to be used.

uniQure's cohort 4 is currently recruiting in the USA and examining whether minimal striatal volume is an essential criterion. These findings will provide an important step forward.

13. When can we expect publication of the peer-reviewed topline results?

ST: The publication is being prepared by uniQure, in collaboration with the steering and neurosurgical planning committees. We hope that this will be submitted soon and that the data will be available for the community.

14. How might the duration of the neurosurgery be reduced?

AR: A number of potential approaches are under discussion, including alternative delivery devices that enable infusions at different rates. Further down the line, indwelling catheters could be placed inside the brain under anaesthesia, potentially allowing this part of the surgery to be completed within an hour or so. Because there are no pain receptors in the brain, the patient could then be woken up and could even sit and read a book while the infusions are performed. This is just one example, not necessarily one that will be taken forward, and not the only one being considered.

Appendix: Disclosures

Åsa Petersén, Patrick Weydt, Ignacio Muñoz-Sanjuan and Dina De Sousa: No connection with uniQure.

Anne Rosser: 'I am the joint PI for the AMT-130 study in Cardiff. I have contributed to ad hoc advisory boards for the study. I do not have any personal financial interests in the company.'

Sarah Tabrizi: 'In the past year, through the offices of UCL Consultants Ltd, a wholly owned subsidiary of University College London, I have undertaken consultancy services and am on SABs for uniQure. All honoraria for these consultancies were paid through UCL Consultants Ltd and go to UCL and my research. I also run clinical trials sponsored by uniQure and the income goes to UCLH Foundation Hospital Trust.'

Jenna Heilman: 'I am employed by HDYO, an organization who receives the majority of funding for several pharmaceutical companies including uniQure.'