Intracerebroventricular Cerliponase Alfa for Neuronal Ceroid Lipofuscinosis Type 2 Disease: Clinical Practice Considerations From US Clinics

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Contents lists available at ScienceDirect
Pediatric Neurology
journal homepage: www.elsevier.com/locate/pnu

ARTICLE INFO

Article history:
Received 31 December 2019
Accepted 25 April 2020
Available online 4 May 2020

Keywords:
Intracerebroventricular
Cerliponase alfa
Neuronal ceroid lipofuscinosis

ABSTRACT

Background: Neuronal ceroid lipofuscinosis type 2 or CLN2 disease is a rare, autosomal recessive, neurodegenerative lysosomal storage disorder caused by tripeptidyl peptidase 1 deficiency. Cerliponase alfa, a recombinant human tripeptidyl peptidase 1 enzyme, is the first and only approved treatment for CLN2 disease and the first approved enzyme replacement therapy administered via intracerebroventricular infusion.

Methods: A meeting of health care professionals from US institutions with experience in cerliponase alfa treatment of children with CLN2 disease was held in November 2018. Key common practices were

https://doi.org/10.1016/j.pediatrneurol.2020.04.018
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Introduction

Neuronal ceroid lipofuscinosis type 2 or CLN2 disease, a form of Batten disease, is an autosomal recessive, neurodegenerative lysosomal storage disorder caused by deficient activity of the tripeptidyl peptidase 1 (TPP1) enzyme.1-3 Mutations in the TPP1 gene reduce the production or activity of the lysosomal protease TPP1, leading to lysosomal accumulation of undegradable proteins and cellular injury, particularly neurodegeneration.1,2 CLN2 disease is ultrarare, with incidence estimates from 0.15 to 9.0 per 100,000 live births.1

CLN2 disease symptom onset typically begins at age between two and four years, and disease progression is rapid.1,2,5,7 Signs and symptoms can include language delay, intractable epilepsy, ataxia, movement disorders, progressive cognitive and motor decline, and vision loss.1,2,5-7 Death usually occurs by age eight to 12 years.4,6

Cerliponase alfa (Brineura; BioMarin Pharmaceutical Inc, Novato, CA) is the first and only approved treatment for CLN2 disease and slows the decline in motor and language function in symptomatic patients aged three or more years, with 83% of patients continuing to respond after three years.8-10 Cerliponase alfa was first authorized in the United States and European Union in 20178,11 and has since been approved in additional countries worldwide. A recombinant form of human TPP1, cerliponase alfa, is also the first approved enzyme replacement therapy administered by extended duration intracerebroventricular (ICV) infusion.

The ICV route enables drugs to be administered directly into a lateral cerebral ventricle via an implanted device comprising a reservoir and a catheter. Although ICV injection is an established drug administration route for chemotherapy and antibiotics, in use for more than 50 years,12 it is typically a defined course of treatment administered by slow push bolus.13 Conversely, cerliponase alfa treatment is anticipated to be lifelong treatment, with ICV infusions administered once every other week, a dosing frequency based on the TPP1 half-life.14 Each cerliponase alfa infusion lasts approximately 4.5 hours, an extended infusion duration that reduces the risk of infusion-associated reactions.15 Known risks associated with ICV administration include infection, intracerebral hemorrhage, device failure, catheter malpositioning or obstruction, and cerebrospinal fluid (CSF) leakage.1,2,3-5,16-19 The chronic nature of the cerliponase alfa treatment regimen poses unique challenges in achieving successful drug delivery and safe administration.

Owing to the rarity of CLN2 disease, few institutions have experience in its treatment, and the number of patients treated at each institution is low. It is critical for institutions to develop and share practices that support the unique cerliponase alfa administration method and ongoing nature of the treatment, and aim to mitigate infection risk. The objective of this article is to share key clinical practice considerations to facilitate the safe administration of ICV cerliponase alfa in patients with CLN2 disease.

Methods

A multidisciplinary expert group meeting of 14 health care professionals from US medical centers and children’s hospitals with experience in the use of ICV cerliponase alfa was held in November 2018 and included five neurologists, one neurosurgeon, two geneticists, one hospitalist, one registered nurse, and four advanced practice nurses.

The goals of the meeting were to (1) share current practices and processes at institutions managing ICV cerliponase alfa treatment in patients with CLN2 disease; (2) discuss experience of adverse events and complications; and (3) identify key practice considerations for preventing and managing complications associated with ICV cerliponase alfa. The expert group refined their practice recommendations during the drafting of this article.

Current experience and key practices

Drawing on their shared experience, the expert group identified key common practices considered essential for achieving successful infusions and preventing and managing complications associated with ICV cerliponase alfa treatment in patients with CLN2 disease (Table). Flexible practices were also identified that varied across institutions with no group consensus for a preferred approach. These key common practices and flexible practices should be considered by institutions developing their own procedures for ICV cerliponase alfa administration.

Dedicated multidisciplinary team

Cerliponase alfa treatment requires a multidisciplinary team to manage the many aspects of patient and family care. ICV port implantation and maintenance, cerliponase alfa preparation, ICV site preparation and infusion, patient monitoring, side-effect management, and ongoing care for signs and symptoms of CLN2 disease. Most institutions represented by the expert group had a dedicated cerliponase alfa team, varying in composition according to institution-specific needs and the number of patients with CLN2 disease undergoing treatment. Team members could include...
Process development

The expert group strongly encourages each institution to develop their own cerliponase alpha–specific processes that cover each step of patient preparation and infusion administration, drawing on experience from other institutions and refining processes to suit their specific institutional standards and resources. As there are no comprehensive guidelines covering all aspects of cerliponase alpha treatment, staff at institutions that have developed processes and gained experience through treatment of patients with CLN2 disease are also encouraged to share that knowledge with counterparts at other institutions. The expert group was in agreement about the benefits of each team member talking to their respective counterparts (nurse, surgeon, pharmacist, primary physician, and so forth) in other institutions with cerliponase alpha experience when establishing their own processes. This communication is especially important before receiving a patient being

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### TABLE
Summary of Key Common Practices and Flexible Practices

<table>
<thead>
<tr>
<th>Key Common Practices</th>
<th>Flexible Practices</th>
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<tbody>
<tr>
<td><strong>Dedicated team</strong></td>
<td>• Adapt size and composition of team to reflect institution-specific needs and patient numbers</td>
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<tr>
<td>• Develop multidisciplinary team with dedicated team lead and coordinator</td>
<td>• Conduct practice runs of all processes to refine the approach and identify potential problems before implementation</td>
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<tr>
<td><strong>Process development</strong></td>
<td>• Antibiotic-impregnated catheters may be used</td>
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<tr>
<td>• Develop cerliponase alpha–specific processes suited to the institution’s standards and resources</td>
<td>• Take intraoperative photographs of the implanted ICV device to assist team in identifying port dome location</td>
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<tr>
<td>• Promote communication and knowledge sharing with counterparts in other institutions that have cerliponase alpha experience, especially surrounding patient transfers from one treating center to another</td>
<td>• The recommended 5- to 7-day period between implantation and infusion may be shortened, but postoperative edema can make port access difficult</td>
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<td>• Provide team training and regular experience to maintain skills</td>
<td>• Wrapping needed to secure the port-needle connection may be dependent on the ICV device used</td>
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<tr>
<td><strong>Choice of ICV device</strong></td>
<td>• ICV port may be replaced prophylactically after 4 years of single-puncture administrations (approximately 105 punctures)</td>
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<tr>
<td>• Select an ICV device that provides stable positioning of port needle base flush with the scalp during infusion</td>
<td>Institutions can determine their preferred practice for the following:</td>
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<tr>
<td>• Ensure neurosurgical and infusion teams discuss impact of the ICV port design on infusion stability before surgical placement of the ICV device</td>
<td>• Choice of sterile field techniques and products</td>
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<tr>
<td><strong>ICV device access</strong></td>
<td>• Choice of infusion premedication</td>
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<tr>
<td>• Familiarize team with ICV device design and access method before first patient</td>
<td>• Confirmatory checks before initiating cerliponase alpha thawing (to avoid possible drug wastage owing to patient nonattendance or infusion cancellation for reasons such as potential infection or device malfunction)</td>
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<tr>
<td><strong>ICV port replacement</strong></td>
<td>• Person responsible for transfer of cerliponase alpha to patient and infusion line priming</td>
</tr>
<tr>
<td>• Train team and patient’s caregivers to monitor for port CSF leakage</td>
<td>• Frequency of monitoring (CSF sampling and vital signs) can vary according to institution practice</td>
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<tr>
<td>• Replace ICV port in the case of infection or device malfunction (e.g., leakage, occlusion)</td>
<td>• Duration of postinfusion observation and location (inpatient or outpatient) can depend on patient condition and duration of treatment, and available facilities</td>
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<tr>
<td><strong>Preparation and administration processes</strong></td>
<td>• Action regarding cerliponase alpha infusion in the case of patient illness or asymptomatic positive CSF culture should be determined on a case-by-case basis</td>
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<tr>
<td>• Certify infusion team in use of strict aseptic techniques</td>
<td>• Choice of sterile field techniques and products</td>
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<tr>
<td>• Use premedication and concurrent medication to reduce discomfort and infusion reactions</td>
<td>• Choice of infusion premedication</td>
</tr>
<tr>
<td>• If removing hair during infusion site preparation, avoid shaving or hair removal cream</td>
<td>• Confirmatory checks before initiating cerliponase alpha thawing (to avoid possible drug wastage owing to patient nonattendance or infusion cancellation for reasons such as potential infection or device malfunction)</td>
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<tr>
<td>• Refine the infusion process to minimize the number of connections and disconnections and to reduce infection risk</td>
<td>• Person responsible for transfer of cerliponase alpha to patient and infusion line priming</td>
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<tr>
<td><strong>Monitoring and management of potential infection</strong></td>
<td>• Frequency of monitoring (CSF sampling and vital signs) can vary according to institution practice</td>
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<tr>
<td>• Monitor for CNS infection</td>
<td>• Duration of postinfusion observation and location (inpatient or outpatient) can depend on patient condition and duration of treatment, and available facilities</td>
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<tr>
<td>• Monitor vital signs</td>
<td>• Action regarding cerliponase alpha infusion in the case of patient illness or asymptomatic positive CSF culture should be determined on a case-by-case basis</td>
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<tr>
<td>• Delay ICV infusion in the case of potential scalp infection or serious infection</td>
<td>• Choice of sterile field techniques and products</td>
</tr>
<tr>
<td>• Replace ICV device in the case of confirmed CSF infection</td>
<td>• Choice of infusion premedication</td>
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**Abbreviations:**
- CNS – central nervous system
- CSF – cerebrospinal fluid
- ICV – intracerebroventricular

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pediatric neurologists, biochemical geneticists, hematologist-oncologists, neurosurgeons, nurse practitioners, epileptologists, pediatric infusion center nurses, pharmacy infusion specialists, hospitalists, nurse coordinators, psychologists, and child life specialists. Some teams include backup staff to cover for potential absences on infusion days.

The expert group agreed that a dedicated team lead and a coordinator are both essential to facilitate the smooth running of patient and treatment management processes. The team lead is often the attending physician and is therefore able to address medical issues, spearhead coordination, generate buy-in for the process, and create bridges to other services. The team coordinator is usually a nurse who preferably had related experience in the administration of complex therapies. The coordinator is central to developing the cerliponase alpha–specific infusion processes and ensuring their implementation, and is considered critical to the success of the team.
transferred from another facility where the ICV device was implanted or where the patient had received cerliponase alfa, as information about preferred care for that patient improves the transfer experience and care at the new institution for the patient and family.

During protocol development, some institutions conducted practice runs of each process to identify potential problems before implementation. Team training and competency in carrying out each step should be ensured before receipt of the first patient; backup staff should also be trained to cover for absences. As many of the process steps may be unique to cerliponase alfa treatment and patient numbers are generally low, team members and backup staff should regularly participate actively in cerliponase alfa ICV infusions to maintain their skills.

Choice of ICV device

An ICV device consists of an access port implanted in the subgaleal space under the scalp and connected to a catheter inserted into one of the lateral cerebral ventricles. Antibiotic-impregnated catheters were used by some institutions and have been reported to reduce infection rates associated with ventriculoperitoneal shunts.20-22 A single-use administration kit is supplied with cerliponase alfa for accessing the ICV device port and contains a 16-mm, 22-gauge Huber-type, nontouching port needle, two syringes and syringe needles, and an infusion set with inline filter and extension line to withdraw CSF and administer treatment.8

A secure anchor between the port and needle is important for stability during the long cerliponase alfa infusion of approximately 4.5 hours. A stable connection can be affected by the choice of ICV device and can be achieved with an ICV port that allows the port needle to be fully inserted and the needle base to lie flush with the scalp, such as the Codman Holter Hickham reservoir recommended in the cerliponase alfa US prescribing information (USPI)6 (Fig 1). Conversely, the expert group reported difficulties with flat-bottomed ports, such as the Ommaya reservoir, because the limited port depth forces the needle to extend beyond the port dome and prevents the base of the needle from lying flush with the scalp. The protruding needle is then difficult to secure, increasing the risk of the needle being dislodged during the infusion (Fig 1).

Each neurosurgeon and medical center may already have their preferred choices of ICV device that are likely based on prior experience with ICV bolus injections using a butterfly needle and syringe; however, their preferred device may not be optimal for extended cerliponase alfa infusions for the reasons described previously. It is therefore crucial for the infusion team to discuss the choice of ICV device with the neurosurgeon before implantation and ensure that the unique need for a stable connection during cerliponase alfa infusion is a key consideration in device selection.

ICV device access

Before treating the first patient, the neurosurgical and infusion teams should discuss the placement and function of the chosen ICV device. Team members should become familiar with the device structure by handling the device and should experiment with accessing the chosen port using the administration kit provided with the cerliponase alfa8 and practicing on a mannequin with an implanted port when possible. In addition, institutions that are new to cerliponase alfa infusion should consider watching ICV port access and cerliponase alfa administration at an experienced institution either by video or an on-site visit, if permitted by each institution and with the permission of the patient and family. A video showing ICV port access is available by clicking on Fig 2 (online version only).

Once the ICV device is implanted, intraoperative photographs of the port can be provided to assist team members in identifying the dome location before port access. However, teams should be aware that the appearance of the port may be affected by postoperative edema and that ports may shift during the postoperative healing process and as the child grows. In addition, the port dome may appear to flatten over time but will remain palpable.

The recommended time from ICV device implantation to first cerliponase alfa infusion is at least five to seven days to allow time for initial healing, for swelling to subside, and to minimize patient discomfort.6 However, one institution performed a cerliponase alfa infusion the day after device implantation when the circumstances meant a delay was not appropriate; the infusion was well tolerated and without complications other than minor difficulty accessing the device because of postoperative swelling.

There was a variation between institutions and between ICV device type in the wrapping and taping techniques used to secure the port needle and infusion line during the infusion. The flat-bottomed Ommaya reservoir required improvised packing of the space between the port dome and the base of the port needle and additional taping to improve connection stability (see Section Choice of ICV device and Fig 1). One institution used a sterile glue (Cavilon) to stabilize hair around the port and provide a surface for tape to adhere to in a patient with an Ommaya reservoir; but this was not deemed necessary in patients with Codman Holter Hickham reservoirs because the needle base sits flush with the scalp.

ICV port replacement

Repeated puncturing of the access dome during long-term ICV treatment may eventually impair the integrity of the port6 and may theoretically increase the risk of infection or CSF leakage. Port replacement is recommended no later than after four years of single-puncture administrations, which equates to approximately 105 punctures based on drug administration using a single puncture every other week.6 As some infusion sessions can require multiple access attempts, institutions may choose to track the number of punctures via procedure notes, electronic health record systems, or other tracking systems. There was no consensus among the expert group members on whether it is necessary to prophylactically replace an ICV device within 4 years or only if required owing to infection or device malfunction, largely because of the limited duration of experience with cerliponase alfa, which was first approved in 2017. Monitoring of ICV port explantation and sharing of experience are encouraged so that port replacement recommendations can be developed. Both the treatment team and the patient’s caregivers should be trained to monitor for port leakage (Fig 3).

Preparation and administration processes

Strict aseptic techniques

The use of strict aseptic techniques is critical to reducing the incidence of ICV infectious complications.6,13 The dedicated infusion team, including physicians, nurses, and backup staff, should be certified in the use of strict aseptic techniques. Other team members may vary in their experience of aseptic techniques and should also be provided training on maintaining sterile conditions, such as the training undertaken by surgical nurses or neurosurgeons. An observer with expertise in situations requiring strict aseptic technique may be useful in identifying and correcting any nonsterile practices among the team.

Institutions varied in their preferred choice of sterile cleansing products, sterile fields, and the personal protective equipment worn by staff and family members in the infusion room. Most
institutions used multiple aseptic agents, either singularly or in combination, including chlorhexidine, iodopovidone, and alcohol. There was no expert group consensus on the choice of single versus multiple agents, the use of scrubs versus swabs, or the minimum number of uses of each agent. However, a combination of chlorhexidine and iodopovidone for preoperative antisepsis has been reported to reduce the incidence of surgical site infections and bacterial colonizations when compared with either agent alone, and the combination of alcohol with other antiseptic agents is recommended by the Association of Surgical Technologists to achieve both rapid and persistent cumulative antimicrobial activity. Institutions may choose their preferred procedures, but sufficient methods should be used to mitigate infection risk.

Premedication and management of infusion-associated reactions

All institutions administered premedication to reduce infusion-associated reactions and patient discomfort. The cerliponase alfa USPI recommends pretreatment with antihistamines, with or without antipyretics or corticosteroids, 30 to 60 minutes before the start of infusion. The minimum premedication used by the institutions varied according to physician preference or the institution’s standard practice and could include antihistamines (e.g., cetirizine, loratadine; diphenhydramine could be used if the benefit was felt to outweigh the risk of seizures), pain relief (e.g., acetaminophen, ibuprofen, lidocaine cream), antipyretics (e.g., acetaminophen, ibuprofen), anti-inflammatories for hypersensitivity reactions (e.g., ibuprofen, prednisone, methylprednisolone), and antiemetics (e.g., ondansetron). Additional premedications could be added based on patient history, such as sedatives for anxiety or antiepileptics for patients experiencing an increase in seizures during or after infusion.

Teams were prepared to manage infusion-associated reactions, such as by slowing or stopping the cerliponase alfa infusion, administering antiemetics for vomiting, or antipyretics or steroids for fever and/or more serious reactions. No institutions had needed to use epinephrine. Acute seizures during or after infusions were managed using standard approaches to epilepsy care.

Infusion site preparation

On the basis of the group’s clinical experience, most institutions chose to remove hair around the infusion site using an electric hair clipper for easier site access and greater tape adhesion. There was agreement that razors or hair removal creams should not be used owing to the potential for skin abrasions or reactions, although the evidence is equivocal regarding whether shaving or use of depilatory creams increases infection risk. Hair washing practices varied, with some institutions requiring patients’ hair to be washed before attendance, some specifying the use of chlorhexidine shampoo (Hibiclens), and one institution recommending washing hair the night before and again on the morning of the infusion.

Cerliponase alfa preparation and administration

Cerliponase alfa is shipped and stored frozen and, once thawed, must be used within 24 hours if in unopened vials or within 4 hours if in the syringe; thawed cerliponase alfa should not be refrozen. Confirmatory checks required before initiating cerliponase alfa thawing and preparation varied according to each institution’s preference. To avoid possible wastage of prepared drug because of either patient nonattendance, cancellation of the infusion owing to
concern for potential infection, device malfunction, or inability to access the device, some institutions had stringent confirmatory requirements before initiating preparation. The requirements ranged from telephone confirmation of the patient’s intention to attend within two days before the appointment or confirmation that the patient is en route to their appointment on the day of the infusion, through to confirmation of clear CSF or visual port inspection, and could be adjusted to patient- and institution-specific circumstances. Cerliponase alfa thawing and preparation time varied from 60 to 90 minutes, which was thought to reflect differences in pharmacy facility ambient temperature. Some institutions held a backup dose of cerliponase alfa on-site so that, in the event of any problems leading to a delay in infusion after initiating the cerliponase alfa thawing or problems with product handling or inspection, the patient could still receive treatment.

In institutions with multiple pharmacies, factors considered when selecting the pharmacy to prepare cerliponase alfa included availability of a sterile hood, familiarity with preparation and transfer of drug product under aseptic conditions, and ability to expedite preparation owing to the instability of the product. There was no expert group consensus as to which team members should be responsible for delivery of the thawed cerliponase alfa to the patient (e.g., pharmacist or nurse) and which team members should prime the infusion line (e.g., pharmacist, nurse, or clinician). In most institutions, the infusion line was primed by the nurse or clinician accessing the port; in the other institutions, the line was primed by the pharmacist after thawing the cerliponase alfa in the pharmacy.

The expert group agreed that the infusion process should minimize the number of connections and disconnections to reduce the likelihood of contamination. Some institutions used a one-way neutral displacement connector (MicroClave) that omits the need for recapping or clamping the port needle tubing after drawing CSF and allows efficient switching between the CSF syringe and primed cerliponase alfa infusion line.

**Monitoring and management of potential infections**

**Patient monitoring**

Monitoring for CNS infection was performed by all institutions at each patient contact. However, there was a variation in the monitoring protocol between each institution, which ranged from visual inspection of the port site or CSF specimen through to CSF analysis of cell count and differential, protein, glucose, and culture. Increased CSF protein and nucleated cells were noted in some patients without signs of infection, but such observations require more systematic evaluation. Routine CSF sampling for cell count and culture is recommended in the cerliponase alfa USPI for infection monitoring before each infusion and when clinically indicated. Most institutions sampled CSF from each patient before every infusion. One institution sent CSF for culture only if the patient had clinical symptoms that could not be explained by known causes. Propionibacterium acnes is one of the common pathogens in implanted devices but is not reliably detected in aerobic culture owing to its slow growth, therefore prolonged aerobic and anaerobic culture for 14 days is recommended.

It is recommended to monitor vital signs before infusion, periodically during infusion, and after infusion. Institution practices for recording vital signs ranged from twice per infusion (once before and once after infusion) up to 12 times per infusion (within 1 hour before, every 30 minutes during, and at 30 minutes and 1 hour after infusion).

For most institutions, patients remained in the same location during cerliponase alfa administration and postinfusion monitoring. The location varied depending on the facilities available and the patient’s needs. Locations were equally divided between inpatient and outpatient facilities, although some patients were participants in clinical trials requiring inpatient care. Some institutions treated outpatients in inpatient facilities if these provided separate rooms for cohorting of infusion patients; this minimizes foot traffic to reduce infection risk and limits patient activity that could jeopardize the continuity of the cerliponase alfa infusion.

**Potential or confirmed infections and illness**

Few institutions had experienced positive CSF test results in cerliponase alfa–treated patients. The expert group concluded that the response to a positive CSF culture should be determined on a case-by-case basis in consultation with the neurosurgeon and infectious disease clinicians, taking into consideration the type of organism and the patient’s symptoms and blood cell count. A positive culture from a CSF sample may indicate contamination rather than an infection, and a second sample should be taken to confirm whether an infection is present, even if the cerliponase alfa infusion has already been completed. Although some experts preferred to immediately recall the patient for a second CSF sample and antibiotic treatment, other experts felt it may be acceptable to monitor an asymptomatic patient before deciding a course of action.

If CSF infection is confirmed by a second positive CSF sample, then treatment with an appropriate antibiotic and removal of the ICV device, including the catheter, are recommended. A new ICV device can be placed on the same or contralateral side. The Infectious Diseases Society of America guidelines should be consulted regarding the treatment of port infections according to the specific flora or bacteria. The expert group agreed that cerliponase alfa infusion should be delayed in the case of potential scalp infection or serious infection. No overall recommendation could be made about whether to infuse cerliponase alfa treatment while awaiting confirmation of asymptomatic CSF infections. No overall recommendation could be made about whether to infuse cerliponase alfa in a patient who was otherwise unwell (e.g., influenza). Some experts argued that continuing treatment may be of benefit in patient recovery. Other experts raised concerns about the ability to recognize and treat potential infusion reactions in the context of illness. However, the group agreed that the decision should be made on a case-by-case basis.

**Postinfusion observation**

Postinfusion monitoring of the patient for symptoms such as fever, vomiting, or lethargy was conducted by all institutions. Some institutions tapered the degree of monitoring over time, completing each patient’s initial infusions in intensive care units or admitting patients overnight as inpatients, then subsequently progressing to monitoring in outpatient settings. The longer initial period of stay is partly to observe how the patient reacts to the treatment but, importantly, allows time to educate and prepare the parents or guardians for possible infusion reactions. Outpatient length of stay postinfusion varied from 30 minutes to 4 hours, but experts caution that infusion-associated hypersensitivity reactions can manifest or escalate at any time after an infusion, even if previous infusions have been uneventful. The duration of postinfusion observation and any family housing requirements should be considered when scheduling treatment.
Conclusions

Best practices for ICV bolus injection over a short-term treatment period are also applicable to the long infusion time and chronic nature of cerliponase alfa treatment, but with some notable differences. As already described, flat-bottomed ICV ports such as the Ommaya reservoir are suitable for ICV bolus injection but do not provide a sufficiently stable connection between port and needle for the 4.5-hour ICV infusion required for cerliponase alfa (Fig. 1). In contrast to the best practice recommendations for short-term ICV treatment, the expert group found that hair removal creams can cause skin irritation and potential infection risk with repeated use and therefore do not recommend their use during chronic ICV treatment with cerliponase alfa.

Acknowledgments

BioMarin Pharmaceutical Inc (10.13039/100008484) sponsored and organized the expert group meeting. Assistance with manuscript preparation including formatting and editorial support was provided by a medical writer who was paid by the sponsor. Editorial assistance with development of these documents was provided by medical writers (Linda Donnini, PhD, CMP, and Serina Stretton, PhD, CMP, of ProScribe—Envision Pharma Group), who did not contribute to the intellectual content. J.C.-P., D.C., and F.L.-P. are employees of BioMarin. Author contributions: J.C.-P., D.C., and F.L.-P. planned the advisory board meeting and topics to be covered. All authors substantially contributed to discussions at the meeting and the subsequent development of an outline and the first draft of the article. All authors critically revised the manuscript and approved the final version, and all vouch for the accuracy of the work, as per International Committee of Medical Journal Editors authorship guidelines.

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