Site and Participant Perspectives on Participating in an ALS Trial Designed to Reduce Burden: COURAGE-ALS

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Disclosures

• SAR is an employee of and owns stock in Cytokinetics
Global study to recruit 555 participants from 16 countries and 85 sites

ALS participants with:
• FVC ≥65.0%
• Symptoms ≤24 months
• ALSFRS-R ≤44

(N=555)
Randomization 2:1
Stratification: Riluzole & Edaravone

Reldesemtiv 300 mg po BID
Placebo
Reldesemtiv 300 mg po BID

End of Study

ClinicalTrials.gov ID: NCT04944784.
ALSFRS-R, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale;
ALSAQ-40, ALS Assessment Questionnaire 40; BID, twice daily; FU, follow-up; FVC, forced vital capacity; po, orally; W, week.
COURAGE-ALS

• Trial design included 2 interim analyses
• The trial was terminated due to futility following the 2nd interim analysis in March 2023
• When the trial was prematurely stopped, 486 participants had been randomized and dosed
• Trial results will be presented on Thursday, December 7 (Session 6B, Clinical Trials)

ClinicalTrials.gov ID: NCT04944784.
Key Features Incorporated to Reduce Participant Burden

• 9 out of 17 visits were scheduled to be done solely remotely
  − All participants were provided a mobile device and a home spirometer
  − Key assessments performed at these visits included
    ▪ Review of adverse events
    ▪ Medication review
    ▪ ALSFRS-R
    ▪ FVC
    ▪ Sampling of blood and urine (not on the same day as above assessments)

• In addition, other than Screening and Day 1
  − Scheduled clinic visits could be converted to a remote visit with approval of the medical monitor
  − If unscheduled lab was needed, it could be drawn remotely

• ALSAQ-40 filled out on an app on the provided device

• Fewer muscles were tested with hand-held dynamometry (HHD) compared with prior trials

ClinicalTrials.gov ID: NCT04944784.
Objectives

• Describe site and trial participant impressions of the features designed to reduce the burden of participating in the trial through:
  − Survey of site personnel
  − Qualitative interview with trial participants

• Determine the amount of missing data from outcome measures performed remotely compared with those done in-clinic and the ability to gather ALSAQ-40 results on an app for the first 24-week period of the trial

ClinicalTrials.gov ID: NCT04944784.
Site Survey
Site survey (1)

• When the study was terminated, a link to the survey was sent to site personnel regarding the impact of the trial design related to:
  − Their interest in the trial initially
  − Ability to recruit and retain participants
  − The ease / difficulty of different aspects of the remote visit from the site’s perspective
  − The site’s insights into how they were viewed by the person living with ALS
  − The perceived site workload of remote compared with in-clinic visits

• Survey Monkey with 21 questions, including 1 open-ended
  − Strongly agree, agree, somewhat agree, neither agree or disagree, somewhat disagree, disagree, strongly disagree, not involved in this aspect of the trial

• Survey was sent to Investigator, Study Coordinator, and Trained Evaluator for 80 sites (all enrolled ≥1 participant)

• All data presented in the charts on Slides 9 through 15 are from the Site Survey; responses were provided by site personnel
141 Responses received; multiple respondents served >1 role

Responses Received, n

- Study coordinator: 82
- Investigator: 39
- ALSFRS-R trained evaluator: 43
- HHD/Grip trained evaluator: 41
- FVC trained evaluator: 41

Percentages from different geographies nearly identical to the overall site makeup.
Numbers next to bars indicate number of responses from site personnel.
ALSFRS-R, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; FVC, forced vital capacity; HHD, hand-held dynamometry.
Remote Visits Were Viewed Favorably by Site Personnel When Considering Whether to Participate in COURAGE-ALS

Numbers next to bars indicate number of responses from site personnel.
The Ability to Convert In-Clinic to a Remote Visit Resulted in Your Participants to Being Able to Remain in the Trial With Disease Progression

Numbers next to bars indicate number of responses from site personnel.
Did Any of Your Trial Participants Convert an In-Clinic Visit to a Remote Visit?

- Yes: 86 responses
- No: 33 responses
- Not involved in this aspect of the trial: 22 responses

Numbers next to bars indicate number of responses from site personnel.

Reasons Why an In-Clinic Visit Was Converted to a Remote Visit (check all that apply)

- Disease progression: 70 responses
- Caregiver availability: 22 responses
- Weather: 14 responses
- COVID restrictions: 9 responses
- Transportation limitations: 37 responses
- Other (please specify): 11 responses

a 86 responses received in total.
From the Perspective of Study Personnel, This Study Was Less Time/Labor Intensive Than a Traditional Clinic-based Trial Design

For the Trial Participant, This Study Was Less Time/Labor Intensive Than a Traditional Clinic-based Trial Design

Numbers next to bars indicate number of responses from site personnel.
Your Site’s Participants Liked Having Labs Collected in the Home

Ease or Difficulty of Scheduling At-Home Lab Collection Was Driven Mainly by Where the Participant Lived

Numbers next to bars indicate number of responses from site personnel.
Your Site’s Participants Liked Remote FVCs to Follow Their Breathing More Closely

What Were the Obstacles for Participants Performing Remote FVCs (check all that apply)

Numbers next to bars indicate number of responses from site personnel. FVC, forced vital capacity.
Qualitative Participant Interview
Qualitative Participant Interviews

• Conducted as part of the original trial design
• Limited to 50 English-speaking participants from 24 trial sites in the US
• Interviewed in the 2 weeks prior to Week 24
  - All participants were still on blinded study drug at the time of the interview
• Although not the primary purpose of these interviews, some of these participants were asked about:
  - Influence of the trial design on their decision to participate
  - How easy / difficult they found the remote visits, including using the provided devices
  - Experience with some of the in-clinic assessments
## Feedback From Participants Regarding Clinical Trial Procedures and Testing

<table>
<thead>
<tr>
<th>Test or Procedure</th>
<th>N</th>
<th>No. Concerns, n (%)</th>
<th>Concerns, n (%)</th>
<th>Nature of Concern</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-clinic FVC</td>
<td>32</td>
<td>28 (88)</td>
<td>4 (12)</td>
<td>Difficult to keep exhaling when out of air (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anxiety about the result (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mouthpiece is too big (1)</td>
</tr>
<tr>
<td>Remote FVC</td>
<td>43</td>
<td>26 (60)</td>
<td>17 (40)</td>
<td>Connectivity or app problems (10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Couldn’t get proper reading (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Concerns about accuracy of measurement (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Problem with mouthpiece (2)</td>
</tr>
<tr>
<td>Overall impression of remote visits</td>
<td>24</td>
<td>17 (71)</td>
<td>7 (29)</td>
<td>Difficulties getting the phone to work (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Connectivity problems (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not good cell reception where patient lives (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Technology problem – unspecified (1)</td>
</tr>
<tr>
<td>ALSAQ-40 app</td>
<td>29</td>
<td>12 (41)</td>
<td>17 (59)</td>
<td>Did/could not answer on mobile device (13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Did not like questions or response options (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Connectivity problems (1)</td>
</tr>
<tr>
<td>HHD testing</td>
<td>25</td>
<td>24 (96)</td>
<td>1 (4)</td>
<td>Disappointed strength decreased; surprised limited testing</td>
</tr>
</tbody>
</table>

ALSAQ-40, ALS Assessment Questionnaire 40; FVC, forced vital capacity; HHD, hand-held dynamometer.
Remote Visits Compared with In-Clinic Visits

• 13 of the 31 participants who were asked reported that the availability of remote visits influenced their willingness to participate in the trial
  − I could never have gone to the city once a month. The fact that they could come [to my] home was great

• Regarding telemedicine contact and home lab
  − I can’t tell you what a convenience it is. It’s just, so great… They should have more trials like that
  − It’s a much more relaxed atmosphere being at home and just sitting in my chair with the phone propped up and just talking and sharing
  − The remote visits certainly made the trial a lot simpler to maintain

• Travel time to the clinic was the aspect most often mentioned as a negative, followed by the duration of the study visit after arriving at the clinic
Assessments: In-Clinic and Remote Visits
Assessment Completion Rates: Remote Compared With In-Clinic

Scheduled events from Day 1 through Week 24

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Completed, n (%)</th>
<th>P Value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lab</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote(^b) (N=1638)</td>
<td>1539 (94)</td>
<td>(P=0.56)</td>
</tr>
<tr>
<td>Clinic(^c) (N=1670)</td>
<td>1577 (94)</td>
<td></td>
</tr>
<tr>
<td><strong>FVC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote(^d) (N=2846)</td>
<td>2340 (82)</td>
<td>(P&lt;0.0001)</td>
</tr>
<tr>
<td>Clinic(^b) (N=1670)</td>
<td>1611 (96)</td>
<td></td>
</tr>
<tr>
<td><strong>ALSFRS-R</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote(^e) (N=1176)</td>
<td>1149 (98)</td>
<td>(P=0.97)</td>
</tr>
<tr>
<td>Clinic(^c) (N=1670)</td>
<td>1632 (98)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Comparison of completion rates between remote and in-clinic visits. \(^b\) Weeks 2, 8, 16, and 20. \(^c\) Day 1, Weeks 4, 12, and 24. \(^d\) Day 1, Weeks 4, 8, 12, 16, 20, and 24. \(^e\) Weeks 8, 16, and 20.

ALSFRS-R, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; FVC, forced vital capacity.
Utilizing a Mobile App for ALSAQ-40

• Background
  - ALSAQ-40 obtained at visits planned to be done in the clinic at Day 1, Week 12, and Week 24
  - App for the ALSAQ-40 was on the trial-provided mobile phone
  - Participants were instructed to bring the phone to all clinic visits
  - Paper form for ALSAQ-40 was used if the phone was forgotten or if the participants could not use the app

<table>
<thead>
<tr>
<th>ALSAQ-40</th>
<th>Day 1</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completion rate, n (%)</td>
<td>483 (99)</td>
<td>413 (99)</td>
<td>310 (97)</td>
</tr>
<tr>
<td>Completed in app, n / N total (%)</td>
<td>218 / 483 (45)</td>
<td>226 / 413 (55)</td>
<td>176 / 310 (57)</td>
</tr>
</tbody>
</table>

ALSAQ-40, ALS Assessment Questionnaire 40.
Conclusions

• Sites and participants both endorsed the inclusion of remote visits in ALS clinical trials
• For sites, this did not necessarily mean less work
• Performing outcome measures remotely or using a mobile phone app had some limitations
  − There were more missed assessments for FVCs done remotely compared with those done in clinic
  − Approximately half of the time, the ALSAQ-40 was completed on paper instead of using the app
  − Harder to identify personnel to go to the home to obtain lab specimens when the participant lived in a remote location
  − Four sites were not permitted by their institution to use the home lab service
• Variability in technological skills and degree of weakness may have played a role in using the portable spirometer and the mobile phone for filling out the ALSAQ-40
Acknowledgments

We thank the participants of COURAGE-ALS and their families for their contributions to this clinical trial.

We also extend our thanks to the investigators and site staff of COURAGE-ALS for their work on the trial and for participating in the site survey.

Funding

The COURAGE-ALS study was funded by Cytokinetics. Participant interviews were conducted by RTI-Health Solutions and were funded by Cytokinetics. Editorial support for the preparation of this presentation was provided by Engage Scientific Solutions and was funded by Cytokinetics.
## Results: Obtaining Assessments Remotely

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Week 2 (n=462)</th>
<th>Week 8 (n=458)</th>
<th>Week 16 (n=376)</th>
<th>Week 20 (n=342)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab</td>
<td>453 (96)</td>
<td>423 (86)</td>
<td>347 (88)</td>
<td>316 (86)</td>
</tr>
<tr>
<td>FVC</td>
<td>NA</td>
<td>369 (81)</td>
<td>296 (79)</td>
<td>275 (80)</td>
</tr>
<tr>
<td>ALSFRS-R</td>
<td>NA</td>
<td>446 (97)</td>
<td>369 (98)</td>
<td>334 (98)</td>
</tr>
</tbody>
</table>

Data are shown as n (%).

ALSFRS-R, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; FVC, forced vital capacity.
# Results: Obtaining Assessments in the Clinic

## Completion Rates for Outcome Measures Associated With In-Clinic Visits

<table>
<thead>
<tr>
<th></th>
<th>Day 1 (N=486)</th>
<th>Week 4 (n=448)</th>
<th>Week 12 (n=418)</th>
<th>Week 24 (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lab</strong></td>
<td>486 (100)</td>
<td>441 (98)</td>
<td>371 (89)</td>
<td>279 (88)</td>
</tr>
<tr>
<td><strong>FVC – in clinic</strong></td>
<td>486 (100)</td>
<td>444 (99)</td>
<td>385 (92)</td>
<td>296 (93)</td>
</tr>
<tr>
<td><strong>FVC – remote</strong></td>
<td>415 (85)</td>
<td>403 (90)</td>
<td>341 (82)</td>
<td>241 (76)</td>
</tr>
<tr>
<td><strong>ALSFRS-R</strong></td>
<td>485 (100)</td>
<td>446 (100)</td>
<td>397 (95)</td>
<td>304 (96)</td>
</tr>
<tr>
<td><strong>HHD</strong></td>
<td>484 (100)</td>
<td>447 (100)</td>
<td>413 (99)</td>
<td>313 (98)</td>
</tr>
<tr>
<td><strong>Grip</strong></td>
<td>484 (100)</td>
<td>447 (100)</td>
<td>413 (99)</td>
<td>311 (98)</td>
</tr>
</tbody>
</table>

Data are shown as n (%).

*a Remote FVC performed ±2 days of in-clinic visit.
ALSFRS-R, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; FVC, forced vital capacity; HHD, hand-held dynamometer.
### Frequency of Converting In-Clinic Visits to Remote Visits

<table>
<thead>
<tr>
<th>Visit</th>
<th>In-Clinic Visits Planned, N</th>
<th>Performed In-Clinic, n (%)</th>
<th>Performed Remotely, n (%)</th>
<th>Missed Visits, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>486</td>
<td>448 (92)</td>
<td>32 (7)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Week 12</td>
<td>460</td>
<td>418 (91)</td>
<td>32 (7)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Week 24</td>
<td>363</td>
<td>318 (88)</td>
<td>24 (7)</td>
<td>21 (6)</td>
</tr>
</tbody>
</table>
Limiting Strength Testing to Grip and HHD of the Hand Muscles Was Better Tolerated by Participants Compared With Testing Multiple Muscles in 4 Extremities Done in Other Trials.

Numbers next to bars indicate number of responses from site personnel. HHD, hand-held dynamometry.