Pharmacotherapy for pulmonary sarcoidosis: A delphi consensus study

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Received 7 October 2009; accepted 20 December 2009
Available online 20 January 2010

Summary

Background: Most issues concerning pharmacotherapy of pulmonary sarcoidosis have not been resolved in clinical trials. The objective was to survey sarcoidosis experts concerning the treatment of pulmonary sarcoidosis and attempt to reach a consensus by these experts using a Delphi method.

Methods: A 6-item questionnaire was developed. Experts were identified at the Diffuse Lung Disease Network at the annual CHEST meeting in October 2008. Three rounds of questionnaires were presented to the experts. Respondent feedback and supporting literature was incorporated into the questionnaires of subsequent rounds.

Results: Experts reached a consensus concerning the following issues: (a) corticosteroids are the initial therapy of choice; (b) initial use of inhaled corticosteroids are not recommended; (c) methotrexate was the preferred second-line drug; (d) 40 mg of daily prednisone equivalent was the maximum dose recommended for the treatment of acute pulmonary sarcoidosis; (e) tapering to 10 mg of daily prednisone equivalent for chronic pulmonary sarcoidosis was considered a successful taper. The experts could not resolve the following issues: (a) the initial corticosteroid dose for the treatment of acute pulmonary sarcoidosis; (b) the decision and timing of corticosteroid therapy in a patient with mild, Stage 2 pulmonary sarcoidosis.

Conclusions: This Delphi study revealed that sarcoidosis experts reached a consensus concerning several aspects of the treatment of pulmonary sarcoidosis; these could be considered as appropriate approaches to therapy. Other issues concerning the therapy of pulmonary sarcoidosis remain unresolved by experts, and are areas where further clinical research could be directed.

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Abbreviations: ICS, inhaled corticosteroids; ATS/ERS/WASOG, the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders.

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Introduction

Pulmonary sarcoidosis is a systemic, granulomatous disease with a variable clinical course. Because of this clinical variability, treatment is not mandated in all cases. Corticosteroids modify the granulomatous inflammation and are considered the medications of choice for pulmonary sarcoidosis. However, there are no clear guidelines for initiating corticosteroid therapy, determining when corticosteroid therapy has failed, and for considering an alternative medication for the treatment of pulmonary sarcoidosis.

The lack of standardization concerning the treatment of pulmonary sarcoidosis results from inadequate clinical trials. Most published studies have involved few subjects, used varying corticosteroid doses or durations, used variable endpoints, and have often not been blinded, randomized, or controlled.

This inadequate rigorous trial data makes consideration of a Delphi research technique reasonable. A Delphi method of polling an expert panel may enable a consensus to be reached in situations where there are inadequate data to determine an objective answer. The aim of this study was to perform a Delphi study of sarcoidosis experts concerning the treatment of pulmonary sarcoidosis using rigorous Delphi study methods including iterative questioning and feedback from previous responses, and to formulate a consensus by these experts whenever possible.

Methods

This study was approved by the Institutional Review Board of the Medical University of South Carolina.

A modified Delphi method was used in this study in an effort to reach a consensus among the experts. The key aspects of Delphi studies include repeated expert questioning, anonymous responses, and feedback from respondents. Multiple-choice questions were used to shorten the time necessary to reach consensus versus proposing open-ended questions.

An initial 6-item questionnaire, with additional questions concerning the experts’ clinical experience, was developed for distribution. All 6 questions concerned the medical treatment of pulmonary sarcoidosis. The survey was limited to 6 questions to encourage a high response rate. All respondents, except for 2, attended the Diffuse Lung Disease Network meeting at the annual American College of Chest Physicians (CHEST) meeting in October 2008 in Philadelphia, PA. An announcement was made during the meeting concerning the study, and a hard copy of the questionnaire was distributed. In addition, the form requested that each participant supply a contact email address. Participants completed the initial questionnaire at the conclusion of the meeting and it was collected by the distributor. Two additional internationally renowned sarcoidosis experts were recruited and completed the initial questionnaire via e-mail. The sarcoidosis experts are listed in Appendix 1.

Subsequent questionnaires were disseminated by email to all the experts. Feedback from respondents was considered and incorporated into revisions of the questions. As is recommended in Delphi studies, the experts were encouraged to supply literature, data, and rationale for their responses that were distributed back to the group anonymously. The experts were also allowed to comment on the questions in terms of their validity, specificity, and content. The feedback from each expert was provided to the entire group when the next questionnaire was disseminated. Respondents had access to the anonymous responses of all the experts from previous questionnaire rounds. Such anonymity is essential in Delphi studies to prevent bias by influential clinicians and to reduce the pressure to conform to a group. The goal of a Delphi study is to reach a consensus. At least 70% agreement of respondents has been proposed to represent a consensus, therefore, this criterion was used in this study.

Three to 5 question rounds are most often performed in Delphi studies. Three rounds were planned for this Delphi study with the option of performing additional rounds if necessary to reach a consensus.

Results

Characteristics of the experts

Table 1 displays the characteristics of the respondents. Thirty-six respondents completed Round #1 of the questionnaire. Almost all (25/28, 89%) had completed training for at least 5 years. The majority of respondents treated more than 25 sarcoidosis patients per year (22/34, 65%) and

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of respondents (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number years since completed training</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>3</td>
</tr>
<tr>
<td>5–10</td>
<td>6</td>
</tr>
<tr>
<td>10–20</td>
<td>8</td>
</tr>
<tr>
<td>&gt;20</td>
<td>10</td>
</tr>
<tr>
<td>No response</td>
<td>9</td>
</tr>
<tr>
<td>Number of patients treated on average</td>
<td></td>
</tr>
<tr>
<td>with sarcoidosis per year</td>
<td></td>
</tr>
<tr>
<td>0–25</td>
<td>12</td>
</tr>
<tr>
<td>25–50</td>
<td>10</td>
</tr>
<tr>
<td>50–100</td>
<td>3</td>
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<td>&gt;100</td>
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<tr>
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<td>2</td>
</tr>
<tr>
<td>Number of clinical trials involved with sarcoidosis</td>
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</tr>
<tr>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>1–3</td>
<td>10</td>
</tr>
<tr>
<td>&gt;3</td>
<td>4</td>
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<tr>
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<td>4</td>
</tr>
<tr>
<td>Number of publications authored concerning sarcoidosis</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>1–10</td>
<td>14</td>
</tr>
<tr>
<td>10–20</td>
<td>2</td>
</tr>
<tr>
<td>&gt;20</td>
<td>3</td>
</tr>
<tr>
<td>No response</td>
<td>4</td>
</tr>
</tbody>
</table>
had been involved in at least 1 sarcoidosis publication (20/33, 59%). Almost half of the experts had been involved in at least 1 clinical sarcoidosis trial (14/32, 44%). The majority of respondents (33/36, 92%) indicated pulmonary/critical care medicine as their subspecialty area of practice, with 3 noting their subspecialty practice as interstitial lung disease, sarcoidosis, or transplant.

Round #1

The 6 questions and experts’ responses are shown in Table 2.

Question #1: You determine that a patient should be treated for pulmonary sarcoidosis. What is your initial starting medication? \((n = 36)\)

- Corticosteroids (33, 92%)
- Methotrexate (0)
- Chloroquine (0)
- Hydroxychloroquine (0)
- Azathioprine (0)
- Other (3, 8%) other responses included: inhaled steroids, combination of steroids and methotrexate, and depends on severity, if early with many symptoms would use prednisone and if later in disease would use methotrexate or hydroxychloroquine

Question #2: For question 1, what is your initial daily dose (if you selected corticosteroids, use prednisone-equivalent dosing; if you selected a drug that you do not dose daily then specify the frequency of dosing)? \((n = 36)\)

- 40 mg (10, 28%)
- 20 mg (9, 25%)
- 1 mg/kg (3, 8%)
- 30 mg (2, 5.5%)
- 20–40 mg (2, 5.5%)
- 30–40 mg (2, 5.5%)
- 0.5 mg/kg (2, 5.5%)
- 40 mg every other day (2, 5.5%)
- 0.5–1 mg/kg (1, 3%)
- 1.5–2 mg/kg (1, 3%)
- 40–60 mg (1, 3%)
- Inhaled budesonide 1600mcg (1, 3%)

Question #3: A 40-year-old woman presents with mild dyspnea and cough. Spirometry reveals a FVC 71% of predicted, FEV1 72% of predicted. Her past medical history is not significant. She is found to have Stage 2 pulmonary sarcoidosis via CXR. Assume that there is essentially no change in her spirometry or symptoms for the foreseeable future, when do you initiate SYSTEMIC (ORAL OR INTRAVENOUS) treatment for pulmonary sarcoidosis? \((n = 30)\)

- Now (11, 37%)
- I would never give that patient a trial of systemic therapy if spirometry and symptoms were essentially unchanged (17, 57%)
- In 3 months (1, 3%)
- In 6 months (1, 3%)

Question #4: I would consider corticosteroid treatment of acute pulmonary sarcoidosis a failure if the patient did not respond after 3 months at what daily prednisone equivalent dose? \((n = 36)\)

- 40 mg (20, 56%)
- 20 mg (8, 22%)
- 30 mg (3, 8%)
- 60 mg (2, 6%)
- 40 mg every other day (1, 3%)
- 0.5 mg/kg (1, 3%)
- I do not treat with corticosteroids for the above patient (1, 3%)
- 15 mg (0)
- 10 mg (0)

Question #5: I would consider corticosteroid treatment of chronic pulmonary sarcoidosis a failure if the maintenance daily prednisone equivalent dose could not be tapered lower than: \((n = 36)\)

- 10 mg (15, 38%)
- 20 mg (10, 29%)
- 15 mg (5, 15%)
- 5 mg (3, 9%)
- 7.5 mg (2, 6%)
- 0 mg (1, 3%)
- 40 mg (0)
- 30 mg (0)

Question #6: The second-line agent that I add to corticosteroids or replace corticosteroids with in patients with sarcoidosis who have an inadequate response to corticosteroids is: \((n = 36)\)

- Methotrexate (24, 67%)
- Azathioprine (6, 17%)
- Hydroxychloroquine (2, 6%)
- Indicated more than one response, including methotrexate, hydroxychloroquine, and infliximab (3, 8%)
- Infliximab (1, 3%)
- Chloroquine (0)
- Thalidomide (0)
- Leflunomide (0)

The 6 questions and experts’ responses are shown in Table 2.
Question #1: You determine that a patient should be treated for pulmonary sarcoidosis with oral corticosteroids. Do you simultaneously initiate concomitant inhaled corticosteroids? (n = 29)

No (25, 86.2%)
Yes (3, 10.3%)
Does not use oral corticosteroids (1, 3.5%)

Question #2: What is your initial daily dose of oral corticosteroids for pulmonary sarcoidosis (use prednisone equivalent dosing)? (n = 30)

40 mg regardless of weight (11, 37%)
20 mg regardless of weight (6, 20%)
20, 30, or 40 mg depending on weight (7, 23%)
0.5 mg/kg (3, 10%)
30 mg regardless of weight (2, 7%)
1 mg/kg (1, 3%)

Question #3: A 40-year-old woman presents with mild dyspnea and cough. Spirometry reveals a FVC 71% of predicted, FEV1 72% of predicted, and DLCO 70% of predicted. Her past medical history is not significant. She is found to have Stage 2 pulmonary sarcoidosis via CXR. Assume that there is essentially no change in her spirometry or symptoms for the foreseeable future and you have discussed the pros and cons of corticosteroids with the patient, when do you initiate systemic (oral or intravenous) treatment for pulmonary sarcoidosis? (n = 29)

I would refrain from giving that patient a trial of systemic therapy if spirometry and symptoms were essentially unchanged (15, 51.7%)
Now (8, 27.6%)
I would follow the patient without therapy. If after X months, her symptoms and pulmonary function do not improve, I would initiate corticosteroid therapy:
In 6 months (3, 10.3%)
In 3 months (1, 3.4%)
In 3–6 months (1, 3.4%)
did not indicate duration of waiting period (1, 3.4%)

Question #4: I would consider corticosteroid treatment of acute pulmonary sarcoidosis a failure if the patient did not respond after 3 months at what daily prednisone equivalent dose? (n = 30)

40 mg (23, 77%)
20 mg (4, 13%)
60 mg (2, 7%)
30 mg (1, 3%)
15 mg (0)
10 mg (0)

Question #5: I would consider corticosteroid treatment of chronic pulmonary sarcoidosis a failure if the maintenance daily prednisone equivalent dose could not be tapered lower than: (n = 30)

10 mg (20, 66.7%)
20 mg (3, 10%)
15 mg (3, 10%)
30 mg (2, 6.7%)
5 mg (2, 6.7%)
40 mg (0)
7.5 mg (0)

Question #6: Please rank your top 2 choices for second-line agents that you would add to corticosteroids or replace corticosteroids with in patients with pulmonary sarcoidosis who have an inadequate response to corticosteroids

1st choice — (n = 30)
Methotrexate (25, 83.3%)
Hydroxychloroquine (4, 13.3%)
Azathioprine (1, 3.3%)
Chloroquine (0)
Infliximab (0)
Thalidomide (0)
Leflunomide (0)

2nd choice — (n = 25)
Azathioprine (11, 44%)
Hydroxychloroquine (5, 20%)
Infliximab (4, 16%)
Methotrexate (3, 12%)
Chloroquine (1, 4%)
Myophenolate mofetil (1, 4%)

therapy (reported as prednisone equivalent dosing) ranging from 15 to 60 mg. However, these data can also be interpreted as 94% (32/34) of experts agreed that treatment with greater than 40 mg of daily prednisone equivalent would not provide any additional benefit to the patient. In this sense, a consensus was reached concerning this question. However, the question was reposed to determine if a more definitive dose could be established.

Question #5: similar to question #4, the corticosteroid dose selections were wide. However, 83% (30/36) agreed that a taper of the maintenance prednisone equivalent dose to 10 mg daily is a successful corticosteroid taper for chronic pulmonary sarcoidosis. In this sense, a consensus was reached concerning this question. Nonetheless, the question was reposed in the next round to try to determine if a more definite response could be established.

Question #6: sixty-six percent (23/35) of experts felt that methotrexate was the second-line agent of choice in addition to, or to replace corticosteroids if patients had an inadequate response to corticosteroids alone. Twelve respondents chose azathioprine, hydroxychloroquine, or infliximab as a second-line agent. This question did not reach the specified criteria of 70% to reach a consensus, so it was modified in further rounds.

**Round #2**

The 6 questions and experts’ responses are shown in Table 3.

**Question #1**: because several respondents made comments about ICS in Round #1, this new question was added to the questionnaire. Eighty-six percent of experts (25/29) would not simultaneously initiate concomitant ICS in addition to oral corticosteroids. The question reached a consensus.

**Question #2**: comments to this question in the first round included consideration of weight-based dosing regimens, and therefore, weight-based choices were included in the second round of this question. However, the responses did not reach a consensus, and it was felt that further rounds would unlikely reach a consensus.

**Question #3**: this question was slightly modified based on the experts’ comments to include additional patient characteristics including diffusing capacity and the patient’s awareness of the benefits and potential risks of corticosteroid therapy. Again, there was a significant discordance.
in the responses to this question. It was concluded that a consensus would not be reached concerning this question.

**Question #4:** the actual corticosteroid dose selections again remained wide as with the first round of this question. However, an overwhelming majority (28/30, 93%) of experts agreed that treatment of acute pulmonary sarcoidosis with greater than 40 mg of prednisone daily equivalent would not provide any additional benefit. In this sense, a consensus was reached concerning this question.

**Question #5:** similar to question #4, the actual corticosteroid dose selections again remained wide as with the first round of this question. However, 93% (28/30) agreed that a taper of the maintenance prednisone equivalent dose to 10 mg daily is a successful corticosteroid taper for chronic pulmonary sarcoidosis. In this sense, a consensus was reached concerning this question.

**Question #6:** this question was modified to instruct the experts to rank their second and third-line agents after corticosteroids. Pulmonary sarcoidosis was also specified as the type of sarcoidosis to be treated for this question. Methotrexate was selected overwhelmingly (25/30, 83%) as the second-line drug. A consensus was therefore reached.

A consensus could not be reached concerning a third-line drug.

**Round #3**

The 2 questions and experts’ responses are shown in Table 4.

**Questions A and B:** Although question A was essentially identical to the first part of question #6 in Round #2 which reached consensus, it was reposed in question A so that respondents had a separate question (question B) to respond to their third-line drug choice. This was performed because several experts omitted a third-line agent in Round #2. Again, methotrexate was selected overwhelmingly (25/32, 78%) as the second-line drug and a consensus was reached. There was wide variation in the third-line agent choice so that a consensus could not be reached.

### Consistency of responses

Consistency of answers was assessed as the percent of respondents who changed their answers between Rounds #1 and #2, as shown in Table 5. Although there was significant inconsistency in the responses, the inconsistencies to questions #4, #5, and #6, did not affect the consensuses reached.

### The relationship between experience and responses

In comparing experts who indicated they treated at least 100 patients per year with sarcoidosis (n = 9) to those who treated less than 100 patients per year (n = 27), there were no differences concerning any of the consensuses that were reached (Table 6).

### Discussion

The treatment of pulmonary sarcoidosis is not standardized. This is the result of inadequate clinical trials that are often not placebo-controlled or randomized, have had variable clinical endpoints, and have included a small number of subjects. In such cases where there are insufficient evidence-based data to determine optimal medical therapy, the Delphi technique has been used as a surrogate approach to develop a consensus.

We believe that this Delphi study involved respondents that were pulmonary sarcoidosis experts. More than two-thirds treated greater than 25 sarcoidosis patients per year, nearly half had been involved in at least 1 clinical sarcoidosis trial, and almost two-thirds had been involved in at least one sarcoidosis publication. Furthermore, there were no major differences in the responses of experts who treated at least 100 sarcoidosis patients per year compared to those that treated less than 100 patients per year. This suggests that even though there was significant variation in the degree of clinical sarcoidosis care and research performed by the experts, they were consistent in terms of their opinions.

The response rate in this study ranged from 83 to 100% in all 3 rounds of the questionnaire. Several treatment questions were not posed in this study in an effort to improve

### Table 4 Round #3 questions and responses (n = 32).

<table>
<thead>
<tr>
<th>Question A</th>
<th>Please indicate ONE second-line agent that you would add to corticosteroids or replace corticosteroids with in patients with pulmonary sarcoidosis who have an inadequate response to corticosteroids: (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (25, 78%)</td>
<td></td>
</tr>
<tr>
<td>Azathioprine (3, 9%)</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine (2, 6%)</td>
<td></td>
</tr>
<tr>
<td>Infliximab (2, 6%)</td>
<td></td>
</tr>
<tr>
<td>Chloroquine (0)</td>
<td></td>
</tr>
<tr>
<td>Leflunomide (0)</td>
<td></td>
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<tr>
<td>Thalidomide (0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question B</th>
<th>Please indicate ONE third-line agent that you would add to corticosteroids or replace corticosteroids with in patients with pulmonary sarcoidosis who have an inadequate response to corticosteroids: (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine (13, 42%)</td>
<td></td>
</tr>
<tr>
<td>Infliximab (9, 29%)</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine (5, 16%)</td>
<td></td>
</tr>
<tr>
<td>Methotrexate (2, 6%)</td>
<td></td>
</tr>
<tr>
<td>Chloroquine (1, 3%)</td>
<td></td>
</tr>
<tr>
<td>Mycophenolate mofetil (1, 3%)</td>
<td></td>
</tr>
<tr>
<td>Thalidomide (0)</td>
<td></td>
</tr>
<tr>
<td>Leflunomide (0)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5 Consistency of responses.

<table>
<thead>
<tr>
<th>Percentage of experts that changed responses between Rounds 1 and 2</th>
<th>Percent of experts whose response changed and moved out of consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question #2</td>
<td>25</td>
</tr>
<tr>
<td>Question #3</td>
<td>15</td>
</tr>
<tr>
<td>Question #4</td>
<td>30</td>
</tr>
<tr>
<td>Question #5</td>
<td>57</td>
</tr>
<tr>
<td>Question #6</td>
<td>22</td>
</tr>
</tbody>
</table>

N/A: not applicable.
response rates. Questions were limited to only a number of important treatment-related issues.

This study was able to reach a consensus on several issues concerning the treatment of pulmonary sarcoidosis. First, oral corticosteroids are the recommended initial treatment for pulmonary sarcoidosis. Second, it is not routinely recommended to initiate concomitant ICS along with oral corticosteroids at the time of initial treatment. Third, a consensus was reached that no additional benefit would be achieved by treating acute pulmonary sarcoidosis with more than 40 mg/day of prednisone equivalent. Fourth, a consensus was reached that a taper of corticosteroids to a maintenance dose of 10 mg/day of prednisone equivalent was a successful taper for the treatment of chronic pulmonary sarcoidosis. Finally, methotrexate was the consensus preferred agent for corticosteroid sparing effects or replacement of corticosteroids.

Several questions posed to the sarcoidosis experts did not reach consensus. We would classify these questions as “controversial” and believe that they are important areas for future clinical research. First, the initial treatment dose of corticosteroids for new onset pulmonary sarcoidosis was not resolved. The American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous (ATS/ERS/WASOG) Disorders Consensus Statement on Sarcoidosis recommends 20–40 mg of daily prednisone equivalent as the initial dose for the treatment of sarcoidosis. Using this wide dose range, 75–87% (27/36 in Round #1, 26/30 in Round #2) of the experts agreed, and in this sense a consensus was reached.

Second, the decision to treat or to observe a patient with mild pulmonary sarcoidosis as judged by symptoms, pulmonary function, and chest radiograph was uncertain among experts. As several studies have shown that corticosteroid therapy improves the short term but not long term outcome of pulmonary sarcoidosis, some have advocated observing mild cases of pulmonary sarcoidosis for a period of time. The experts could not resolve this issue. Interestingly, there was an inconsistency between the rounds concerning the experts’ responses that involved corticosteroid dosing. This suggests that even sarcoidosis experts do not have a consistent dose of corticosteroids that they use for the treatment of pulmonary sarcoidosis. It is possible that several experts changed their answers because of feedback to questions from the group. However, it is important to note that this variation was not great enough to alter the consensuses that were reached.

This study has several potential limitations. First, the use of multiple-choice questions can potentially limit responses or induce bias. However, this study encouraged the experts to include a text comment on all questions and allowed for the opportunity to add to the existing responses. These comments from the experts were often incorporated into further rounds of the questionnaire. Second, there was not a complete response of all the experts or to all of the questions. However, the response rate was relatively high with 83–100% of all questions receiving responses. Third, not all of the responders may have been pulmonary sarcoidosis experts. Nevertheless, we demonstrated (Table 6) that the entire group came to a similar consensus as the experts with the greatest clinical

<table>
<thead>
<tr>
<th>Question</th>
<th>Consensus</th>
<th>Experts caring for ≥100 sarcoidosis patients per year who reached consensus, n (%)</th>
<th>Experts caring for &lt;100 sarcoidosis patients per year who reached consensus, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Round 1, Question 1</td>
<td>Corticosteroids are the drug of choice</td>
<td>7/9 (78)</td>
<td>24/25 (96)</td>
</tr>
<tr>
<td>Round 1, Question 4</td>
<td>Acute pulmonary sarcoidosis should not be treated with more than 40 mg/day of daily prednisone equivalent.</td>
<td>7/9 (78)</td>
<td>22/25 (88)</td>
</tr>
<tr>
<td>Round 1, Question 5</td>
<td>A successful taper is to 10 mg/day of daily prednisone equivalent.</td>
<td>8/9 (89)</td>
<td>22/25 (88)</td>
</tr>
<tr>
<td>Round 2, Question 1</td>
<td>ICS is not recommended for initial therapy.</td>
<td>6/8 (75)</td>
<td>17/19 (89)</td>
</tr>
<tr>
<td>Round 2, Question 4</td>
<td>Acute pulmonary sarcoidosis should not be treated with more than 40 mg/day of daily prednisone equivalent.</td>
<td>7/8 (88)</td>
<td>19/20 (95)</td>
</tr>
<tr>
<td>Round 2, Question 5</td>
<td>A successful taper is to 10 mg/day of daily prednisone equivalent.</td>
<td>8/8 (100)</td>
<td>18/20 (90)</td>
</tr>
<tr>
<td>Round 2, Question 6</td>
<td>Methotrexate is 2nd line therapy.</td>
<td>7/8 (88)</td>
<td>17/20 (85)</td>
</tr>
<tr>
<td>Round 3, Question</td>
<td>Methotrexate is 2nd line therapy.</td>
<td>8/8 (100)</td>
<td>16/21 (76)</td>
</tr>
</tbody>
</table>

ICS: inhaled corticosteroids.

a 2 experts did not indicate the number of patients with sarcoidosis they treated per year; 9 experts cared for ≥100 sarcoidosis patients per year; 25 experts cared for <100 sarcoidosis patients per year.
b 7 experts did not respond.
c 6 experts did not respond.
d 5 experts did not respond.
experience. Finally, the majority of the experts practice in the United States. It is possible that these results may not apply to some international populations, as the phenotypic expression of sarcoidosis varies throughout the world.

In conclusion, this Delphi study revealed several aspects of the treatment of pulmonary sarcoidosis which reached a consensus opinion by sarcoidosis experts; these could be considered as appropriate approaches to therapy given the lack of evidenced-based data. Other questions concerning the therapy of pulmonary sarcoidosis remain unresolved by experts, and are areas where further clinical research could be directed.

Acknowledgements

The authors wish to acknowledge the sarcoidosis experts who participated in this study (see Appendix 1). Additionally, we would like to thank Sooyeon Kwon, PhD for her assistance with this manuscript.

All of the authors were significantly involved in the design, data collection, and manuscript preparation concerning this research.

Conflict of interest statement

The authors have no source of financial support for this research study.

Funding

None declared.

Appendix 1

List of experts who completed the questionnaires

Carlo Albera, MD; James Allen, MD; Selim M. Arcasoy.
Robert P. Baughman MD; Kevin K. Brown, M.D.; Roberto G Carbone.
Harold R Collard; Sonye K. Danoff; Joao A. de Andrade; Marjolein Drent.
Linda S. Efferen; Paul Fairman; Stephen K. Frankel; Reda E. Girgis; Kristin B. Highland.
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