Current management of patients hospitalized with complicated skin and soft tissue infections across Europe (2010–2011): assessment of clinical practice patterns and real-life effectiveness of antibiotics (REtrospective Study to Assess the Clinical Management of Patients with Moderate-to-severe cSSTI or CAP Infections in the Hospital Setting [REACH] study)

Javier Garau1, Francesco Blasi2, Jesús Medina2, Marco Avilà3, Kyle McBride4, Helmut Ostermann5, on behalf of the REACH study group

1Department of Medicine, Hospital Universitario de Torrecilla, Barcelona, Spain; 2Respiratory Medicine Section, Università degli Studi di Milano, Milan, Italy; 3Medical Department, AtaxiaZeneca, Madrid, Spain; 4Medical Department, AstaZeneca Europe, Belgium; 5Hostel Services, Inc., Chatham, NJ, USA; 6Department of Internal Medicine III, University Hospital Munich, Munich, Germany.

Background

- Complicated skin and soft tissue infections (cSSTI) are among the most common infections treated in the hospital setting, accounting for up to 10% of all infections treated in both the USA and the United Kingdom (UK).
- cSSTI frequently require intravenous (IV) antibiotic therapy and surgical intervention, and may be further complicated by the presence of significant comorbidities.1,2
- Data on the real-life management of cSSTI and identification of factors predicting for initial treatment modifications and their impact are scarce.3

The REtrospective Study to Assess the Clinical Management of Patients with Moderate-to-severe cSSTI or community-acquired pneumonia (CAP) Infections in the Hospital Setting (REACH) study has systematically collected current (2010–2011) pan-European data on patients hospitalized for cSSTI (clinical trial.govs clinical trials NCT01293435).

- Data on the community-acquired pneumonia (CAP) analyses will be presented in oral presentations UI74 and UI75.

Objective

- To provide current, accurate real-world data on the burden of cSSTI and its clinical management across Europe, by understanding patient and disease characteristics, current clinical practice and disease outcomes.

Methods

Study design

REACH was a multicentre, multinational, retrospective, observational cohort study of patients hospitalized with cSSTI.

- Data were collected via an electronic Case Report Form from 129 sites in ten participating countries across Europe (Belgium, France, Germany, Greece, Italy, the Netherlands, Portugal, Spain, the UK and Turkey) between March 2010 and February 2011.

Inclusion criteria

- The analysis population comprised adults ≥ 18 years of age, hospitalized with cSSTI and requiring IV treatment with antibiotics on admission.
- Patients were required to have:
  - an infection affecting deeper soft tissue and/or requiring significant systemic-vascular intervention
  - infection developing on a lower limb in subjects with diabetes mellitus or well-documented peripheral vascular disease, a major abcess, infected ulcer or deep and extensive cell wall involvement
- In addition, patients were required to exhibit at least two local signs of SSTI present or spontaneous drainage/drainage, erythema, fluctuation, heat/localized warmth, van/wound to palpation, swelling/inflammation) and at least one systemic symptom (temperature (> 38°C), white blood cell count of > 10,000/mm3 or > 10% immature neutrophil).

Exclusion criteria

- Patients with uncomplicated SSTI, such as simple abrasions, impetiginous lesions, superficial ulcers, furunculosis or folliculitis were also excluded, as were patients with cSSTI with a high cure rate after surgical incision alone or after aggressive local skin care.

Data analysis

- This was a retrospective non-interventional study, using a descriptive analysis approach to assess clinical management, clinical outcomes and healthcare resource use. All calculations and summaries were produced using SAS Version 9.2.
- In REACH, ‘Initial treatment modification’ was defined as the need for a change in first-line antibiotic treatment due to insufficient response, adverse reaction, interaction with other drugs, non-suitability of the initial treatment based on the results of microbiological tests (i.e. changes to, or additions of, new agents in a subsequent line (alone or in combination)), patient death, or streaming (de-escalation of treatment to narrow spectrum antibiotic upon patient improvement or confirmed microbiological diagnosis, this represents good clinical practice).

Results

Patient population

- A total of 1966 patients were included in the analysis population, with Spain, Italy and Turkey contributing the largest numbers of patients (Figure 1).
- Patient demographics, characteristics and relevant medical history are shown in Table 1.

Disease characteristics

- The most common types of lesion were cellulitis or fasciitis and abscess (Table 2).
- A total of 701 patients (35.1%) had been treated with antibiotics within 1 week before the index visit or prior to development of cSSTI if already hospitalized.
- Bacteremia was documented in 302 patients (15.1%).
- A total of 279 (14.0%) patients had undergone invasive surgical treatment in the 3 months prior to the index visit.

Table 1: Patient demographics, characteristics and medical history

<table>
<thead>
<tr>
<th>Country</th>
<th>n (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>408 (20.9)</td>
</tr>
<tr>
<td>Italy</td>
<td>211 (10.7)</td>
</tr>
<tr>
<td>Turkey</td>
<td>191 (9.7)</td>
</tr>
<tr>
<td>France</td>
<td>104 (5.3)</td>
</tr>
<tr>
<td>Greece</td>
<td>16 (0.8)</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>14 (0.7)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>11 (0.5)</td>
</tr>
<tr>
<td>Portugal</td>
<td>8 (0.4)</td>
</tr>
<tr>
<td>Germany</td>
<td>6 (0.3)</td>
</tr>
</tbody>
</table>

- A total of 54 different antibiotic agents were used either as monotherapy or in combinations.
- The most frequently chosen initial antibiotic treatments were amoxicillin–clavulanate (n = 366, 18.3%), amoxicillin–sulbactam or sulbactam (n = 150, 7.8%) and piperacillin–tazobactam (n = 135, 6.8%).

Microbiological diagnosis

- All patients underwent a microbiological test, 1059 (53.1%) had a bacteraemia or fungaemia, and 616 (31.0%) had a superficial culturable lesion. A microbiological diagnosis was obtained for 1001 (51.2%) patients (Table 3).

Clinical outcomes

- Clinical outcomes for the full analysis population are detailed in Table 4.
- A high proportion of patients required initial antibiotic treatment modification (51.7%), which included switching in 4.6% and adding in 47.2% of the overall study population. Reasons for treatment modification are presented in Table 5.

Table 4: Clinical outcomes for the full analysis population

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial antibiotic treatment modification, n (%)</td>
<td>1010 (51.7)</td>
</tr>
<tr>
<td>Time to first treatment modification (n = 947), days (median)</td>
<td>7.7 (9.0)</td>
</tr>
<tr>
<td>Overall treatment duration (n = 1075), days (median)</td>
<td>14.6 (14.3)</td>
</tr>
<tr>
<td>Time to clinical stability (n = 1178), days (median)</td>
<td>9.7 (11.2)</td>
</tr>
<tr>
<td>Length of hospital stay (n = 1444), days (median)</td>
<td>18.0 (20.0)</td>
</tr>
<tr>
<td>Discharged from hospital, n (%)</td>
<td>1862 (94.3)</td>
</tr>
<tr>
<td>Reinfection or recurrence, n (%)</td>
<td>172 (8.6)</td>
</tr>
<tr>
<td>Home-care based after discharge, n (%)</td>
<td>282 (12.7)</td>
</tr>
<tr>
<td>Length of home-care stay (n = 138), days (median)</td>
<td>30.8 (15.0)</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>63 (3.2)</td>
</tr>
</tbody>
</table>

Table 5: Reasons for initial antibiotic treatment modification

- Patients with comorbidities (n = 1557), ep. diabetes (33.9%), peripheral vascular disease (21.2%), congestive heart disease (12.2%), cancer or malignancy (10.4%), experienced a higher rate of initial treatment modification than those without (49.3% vs 37.1%) and a longer duration of hospital stay (mean 19.4 days versus 13.2 days).
- Patients with nosocomial SSTI (n = 1860, 90.8%) had a longer time to clinical stability compared with those with a non-nosocomial infection (mean 11.2 days versus 9.5 days), a longer length of hospital stay (mean 30.4 days versus 16.6 days), a higher rate of initial treatment modification (51.3% versus 45.9%) and a higher rate of mortality (4.0% versus 3.3%).
- Patients with a recurrent infection (n = 172, 86.2%) had a longer time to clinical stability than patients without a recurrent infection (mean 12.3 days versus 9.2 days), had a higher rate of initial treatment modification (45.9% versus 44.5%) and required a longer hospital stay (mean 21.9 days versus 17.3 days) than patients with no recurrent initial infection.
- Initial treatment modification rate was higher, compared with the total population, in patients with SSTI with lesions > 50 cm2 (58.0% versus 49.3%)

- Any other relevant medication

Adverse events

- 593 (30.7) episodes of adverse events were reported. The most commonly reported adverse events were infusion reaction (n = 82, 4.1%), other, unknown (n = 246, 12.3%), death (n = 28, 1.4%).

Table 5: Reasons for initial antibiotic treatment modification

- A comparison of the clinical outcomes variables in each participating country shows a geographical variation of initial treatment modification rates (from 33.8% in the Netherlands to 55.6% in Italy), duration of hospital stay (mean of 10.2 days in the Netherlands to 34.1 days in Germany) and percentage of patients admitted to ICU (1.2% in the United Kingdom to 22.0% in Germany).

Conclusions

- This large pan-European study provides important current data characteristics and disease burden of cSSTI and CAP in different European regions.
- The findings reveal the heterogeneity of patients with cSSTI and CAP in different European regions, and provides evidence of a high rate of initial treatment modification.
- The data presented here, and further analysis of the wealth of data accumulated during the REACH study, can be useful in the evidence to assesses and to help recent clinical practice in order to improve patient outcomes.

Author disclosures

- The study was a multicentre, multinational, observational cohort study of patients hospitalized with cSSTI. The study was funded by AstraZeneca, Novartis, Vifor, Pfizer, and B. Braun, among others.
- The study was not funded by any of the authors.
- The authors declare no conflict of interest.

Reference