Table 3 Proposed Initial Treatment and Antibiotic Duration for Invasive Nocardiosis, Based on Clinical Presentation, Before Obtaining Species Identification and/or Antibiotic Susceptibility Testing

Clinical Presentation	Initial Antibiotic Treatment, Antibiotic Duration
Skin*	Monotherapy: cotrimoxazole OR linezolid Antibiotic duration: 3 months. Initial oral treatment is possible.
Pulmonary, non-severe*	Monotherapy: cotrimoxazole OR linezolid Antibiotic duration: 4 to 6 months. Initial oral treatment is possible.
Pulmonary, severe*	Multi-drug regimen: 2 drugs among the 5 first-line agents. Possible combinations include: - [Imipenem OR cefotaxime OR ceftriaxone] + [amikacin OR cotrimoxazole OR linezolid] Antibiotic duration: 4 to 6 months. 2–3 weeks of intravenous therapy.
Central nervous system*	Multi-drug regimen: 2 to 3 drugs among the first-line agents. Possible combinations include: - [Imipenem OR cefotaxime OR ceftriaxone] + amikacin + cotrimoxazole - [Imipenem OR cefotaxime OR ceftriaxone] + [cotrimoxazole OR linezolid] Antibiotic duration: 12 months. 3–6 weeks of intravenous therapy.

Notes: Associated measures: In case of abscess, surgical treatment or radiologic aspiration should be considered. *Based on animal studies and numerous case series; No controlled trials available.

weeks. Conversely, among the 10 patients who completed 4 to 6 months of therapy, only 1 (10%) relapsed and this relapse was due to antibiotic resistance.[63] However, antibiotic doses in this study were in the range of 5–10 mg of trimethoprim (TMP)/kg, which is less than currently proposed dosages (usually 15 mg of TMP/kg per day (see Table 2)).[7,62] More recent data with other antibiotic regimens or higher cotrimoxazole daily doses suggest that the antibiotic duration could be shortened. Tripodi and coworkers described 12 patients with pulmonary nocardiosis after heart transplantation who initially received bactericidal antibiotics (mostly imipenem/amikacin combination) followed by oral drugs for a total of 3 to 4 months of treatment: there were no relapses.[60] More recently, a subset of 17 patients, from 117 with post-solid organ transplant nocardiosis, who received antibiotic treatment for less than 120 days was described;[53] although the median antibiotic duration was 56 [24–120] days, only one patient relapsed.[53] In all these cases, patients received at least 2 weeks of intravenous bactericidal antibiotics. These data suggest that in patients with pulmonary or cutaneous nocardiosis initially treated with bactericidal antibiotics, and who show clinical improvement, the duration of treatment can be reduced to 4 months, especially if the patient experiences antibiotic-related adverse effects.

If there is CNS involvement, treatment is usually maintained for 12 months, although, again, no studies have been conducted to assess shorter durations (Table 3).

Apart from antibiotic therapy, surgical treatment should be considered for deep abscesses, if there is no microbiological diagnosis or if antibiotic treatment alone is not effective, especially if there is CNS involvement.[20]

After completion of antibiotic therapy, secondary prophylaxis may be considered, especially if there is an ongoing immunosuppressive condition. No randomized study has shown a benefit of cotrimoxazole prophylaxis in this setting. Because low-dose cotrimoxazole does not prevent nocardiosis among solid organ transplant recipients, higher doses should be used for secondary prophylaxis, as shown in patients with CGD (eg, 160/800 mg of TMP–SMX daily).[7,14,15,17]

Follow-Up and Prognosis

No data have been published to describe how quickly a patient with nocardiosis should improve after initiating antibiotic treatment; the following proposals are therefore based on expert opinion. Apyrexia is usually achieved after a few days of antibiotic treatment and skin lesions improve within weeks. Follow-up imaging focusing on the body site that was initially infected is mandatory to study the patient's response to treatment. During follow-up, clinical or radiological worsening should encourage consideration of several possibilities. First, treatment failure may be caused by antibiotic under-dosing, poor adherence to treatment, interaction with other treatments, or poor distribution of antibiotics to infected sites. Therapeutic drug monitoring can be performed to rule out these hypotheses. Second, treatment failure may occur if the *Nocardia* isolate is resistant to the prescribed antibiotics, again highlighting the importance of continuous collaboration between physicians and clinical microbiologists. The presence of co-infections, defined as additional microbial pathogens identified at the time of nocardiosis diagnosis, should also be investigated if the patient's condition worsens despite the use of effective antibiotics. The likely types of co-infection will depend on the geographical area and a patient's underlying conditions. For example, among 117 post-solid organ transplant patients with