



**KEY POINTS**

- Increasing global spread.
- Growing number of international outbreaks.
- Attention needed for early detection and identification.
- Intense infection control measures and attention to environmental cleaning should be given at first detection of *C. auris*.

animal models [22]. The time from hospital admission to onset of candidemia with *C. auris* has been reported to range between 9 and 62 days [4,5<sup>■</sup>,15<sup>■</sup>,18<sup>■</sup>,23,24<sup>■</sup>]. The delayed occurrence of candidemia suggests a nosocomial acquisition and spread [3<sup>■</sup>,15<sup>■</sup>,18<sup>■</sup>,25<sup>■</sup>].

The overall crude 30 day in-hospital mortality rate from *C. auris* candidemia in case series ( $n > 1$ ) ranges from 33 to 72% [5<sup>■</sup>,15<sup>■</sup>,18<sup>■</sup>,26<sup>■</sup>]. Better survival likelihood was seen for neonates and infants and patients with immediate source control [9,18<sup>■</sup>]. *Candida auris* attributable mortality cannot be established from those studies as underlying medical conditions are severe and because of the multi-drug-resistant nature of *C. auris*. Research from the United Kingdom, however, showed no direct contribution of *C. auris* to death of patients [3<sup>■</sup>].

**ANTIFUNGAL RESISTANCE AND THERAPY**

Although at the moment, no established minimum inhibitory concentration (MIC) breakpoints exist for *C. auris*, initial testing of an international collection of 54 isolates demonstrated that nearly all (93%) isolates were highly resistant to fluconazole based on breakpoints established for other *Candida spp.* [5<sup>■</sup>]. In that study, more than half of *C. auris* isolates were resistant to voriconazole, around one-third (35%) were resistant to amphotericin B (MIC  $\geq 2$ ), and 7% were resistant to echinocandins [4]. Forty-one percentage of isolates were resistant to two antifungal classes and some (4%) isolates have demonstrated elevated MICs to all three major antifungal classes, including azoles, echinocandins, and polyenes, indicating that treatment options would be very limited [5<sup>■</sup>]. Similar findings were reported from Kuwait showing 100% fluconazole, 73% voriconazole and 23% amphotericin B resistance among 56 isolates [27]. A large study with 350 isolates included (75% blood culture isolates) gave a less grim prospect of resistance percentages outside fluconazole. This study reported 90% of *C. auris* being fluconazole-resistant (MICs 32–64 mg/l), 8% amphotericin B-resistant ( $\geq 2$  mg/l), 15% voriconazole resistant

(>1 mg/l) and 2.5% resistant to echinocandins (16 mg/l) [11<sup>■</sup>].

Echinocandin use, therefore, has become more widespread and the go-to drug, although *C. auris* isolates with reduced susceptibility for this drug have been reported [5<sup>■</sup>,28<sup>■</sup>]. Fortunately, several new drugs with activity against *C. auris* are becoming available. The 1,3- $\beta$ -D-glucan synthesis inhibitor SCY-078 has shown promising antifungal activity against all *C. auris* clades [13<sup>■</sup>,29<sup>■</sup>] as has the new drug APX001 (a GPI-anchored wall transfer protein 1) [30<sup>■</sup>] and rezafungin (previously CD101) a long-acting echinocandin [28<sup>■</sup>]. Unfortunately, the latter drug appears also to be inactive if the newly described substitution S639F in the FKS1 hotspot region is present [11<sup>■</sup>,28<sup>■</sup>]. Elevated echinocandin MICs were associated only with clinical failure if FKS1 mutations are present [31]. In-vitro combination of antifungal drugs against resistant *C. auris* provided some encouraging data [32<sup>■</sup>].

**EPIDEMIOLOGY**

At present, *C. auris* infections, specifically fungemia, have been reported from South Korea [9], Japan [33], India [4], Pakistan [5<sup>■</sup>], South Africa [34], Israel [35<sup>■</sup>], Kuwait [23], Venezuela [18<sup>■</sup>], Colombia [26<sup>■</sup>,36], Panama [37<sup>■</sup>], the United Kingdom [3<sup>■</sup>], Spain [38<sup>■</sup>], Oman [15<sup>■</sup>,16<sup>■</sup>], Canada [39<sup>■</sup>], United Arab Emirates [40<sup>■</sup>], Malaysia [41<sup>■</sup>], the United States of America [42<sup>■</sup>,43<sup>■</sup>], Switzerland [44], and Germany [45]. *Candida auris* has also been identified in Austria, Belgium, China, and France [46,47]. Australia, Kenya, Norway, Russia, Saudi Arabia, Singapore, Thailand, and the Netherlands have reported cases, although detailed or published reports of these cases are not available [45,48<sup>■</sup>,49]. Retrospectively it was found that the reported *C. auris* isolates from Brazil originated from Venezuela. A major outbreak has recently been described in Spain [50]. Figure 1 visualizes the worldwide report of *C. auris* infections. Moreover, official reports and publications on outbreaks will always be one step behind, making it harder to assess the true prevalence and threat of *C. auris* and consequently highlights the need for infection prevention guidelines.

Whilst isolated sporadic cases occur, there is a growing concern regarding the propensity of *C. auris* to cause widespread nosocomial outbreaks [19<sup>■</sup>]. Clusters have been found around the globe [18<sup>■</sup>,24<sup>■</sup>,34,50–52]. In some regions *C. auris* is among the top-3 *Candida* species isolated from bloodcultures [53]. As of August, 2016, the CDC has been accumulating outbreak data in the United States of America. Within the first month, seven cases were recorded [24<sup>■</sup>]. As of 2 March 2018, 215









