# 19 - Management of treatment resistant depression

# Management of treatment-resistant depression – commonly used treatments

348 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Management of treatment--resistant depression – commonly used treatments Resistant depression is difficult to treat successfully and outcomes are often poor,1–3 especially if evidence-based protocols are not followed.4 Treatment-resistant depression is not a uniform entity but a complex spectrum of severity which can be graded5 and in which outcome is closely linked to grading.6 A significant minority of apparently resistant unipolar depression may in fact be bipolar depression,7,8 which is often unresponsive to standard antidepressants9,10 (see section on bipolar depression in Chapter 2). There has been a move to characterise treatment-resistant depression as ‘difficult to treat’ depression on the basis that the former description implies that depression treatments are normally effective and that non-response is therefore somehow abnormal.11 Others suggest abandoning treatment-resistant depression as a diagnosis (again proposing ‘difficult to treat’ depression) because it propels clinicians to try more and more drugs in increasingly complex regimens rather than managing expectations of recovery to a more realistic level.12 Management of treatment-resistant depression has been informed by the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) programme. This was a pragmatic effectiveness study, which used remission of symptoms as its main outcome.13 This study and its various subanalyses have now been somewhat discredited, principally because of high dropout rates after the initial treatment stages. Other criticisms of the STAR*D programme include the absence of a placebo group, the open nature of treatment and some assessments, the failure to account for patients withdrawing after their first visit, the unexplained use of an a priori secondary measure as the main outcome metric, payments made to subjects, and the observation that 93% of 1,518 patients in remission had relapsed or dropped out of the study at 12 months’ follow-up.14,15 In addition to this, reanalysis of

original data collected found the overall remission rate to be 35%, as opposed to the claimed rate of 67%.16 Commonly used drugs for refractory depression that are generally well supported by published literature are shown in Table 3.3. Table 3.3 Commonly used treatments, generally well supported by published literature (no preference implied by order). Treatment Advantages Disadvantages Add aripiprazole17–23 (2–20mg/day) to antidepressant (brexpiprazole and cariprazine are also effective)24–26 ■ ■Good evidence base ■ ■Usually well tolerated and safe ■ ■Low doses (2–10mg/day) may be effective ■ ■Supported by meta-analyses24,27,28 ■ ■Akathisia and restlessness common at standard doses (≥10mg/day) ■ ■Insomnia may be problematic Add lithium29 Aim for plasma level of 0.4–0.8mmol/L initially, increasing to up to 1.0mmol/L if suboptimal response ■ ■Well established ■ ■Well supported in the literature ■ ■Recommended by NICE30 ■ ■Supported by meta-analyses27,28 ■ ■Sometimes poorly tolerated at higher plasma levels ■ ■Potentially toxic ■ ■Usually needs specialist referral ■ ■Plasma level monitoring is essential (Continued)

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