In conclusion, our findings indicate that ELISPOT assays of PBMCs and CSF-MCs are useful adjuncts to current tests for diagnosing TBM. The PBMC ELISPOT assay combined with CSF ADA is a useful rapid rule-out test and the CSF-MC/PBMC ELISPOT ratio is an accurate rule-in test.

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On linezolid efficacy and tolerability

To the Editors:

To further comment on the safety, tolerability and efficacy profile of linezolid in treating ''difficult'' tuberculosis (TB) cases, following the recent study by VILLAR *et al*. [1], we here report on the experience of the E. Morelli Hospital in Sondalo, Italy, a reference centre for difficult-to-treat TB cases, *e.g.* those affected by multidrug-resistant (MDR)- and extensively drug-resistant (XDR)-TB, located in northern Italy [2–3].

As reported elsewhere [3], linezolid has been prescribed ''off label'' in Sondalo, Italy since 2005 to treat patients for whom at least four active drugs cannot be ensured, according to World Health Organization recommendations [4].

Administration of linezolid, within regimens designed to balance efficacy and tolerability, needs to be guided by clear scientific evidence focused on the ideal dosage (per kg body weight per day) and duration [1, 5–9].

The aim of this letter is to describe our recent experience of linezolid tolerability and efficacy between 2009 and 2010.

Methods and definitions are consistent with those used in previous studies by our group [1, 6].

MDR- and XDR-TB have been defined, respectively, as *in vitro* resistance to at least isoniazid and rifampicin (the two most potent first-line drugs for TB treatment) and resistance to isoniazid and rifampicin plus any fluoroquinolone and at least one of the injectable drugs amikacin, capreomycin or kanamycin.

The main results of this study are summarised in tables 1–3.

TABLE 1 Epidemiological characteristics of 12 patients with multidrug-resistant/extremely drug-resistant (XDR) tuberculosis (TB) treated with linezolid in Sondalo, Italy

XDR-TB	4/12 (33)
Resistance to streptomycin	10/12 (83)
Resistance to ethambutol	9/12 (75)
Resistance to pyrazinamide	9/12 (75)
Resistance to fluoroquinolones	7/12 (58)
Resistance to amikacin	3/12 (25)
Resistance to kanamycin	6/11 (54)
Resistance to capreomycin	3/11 (27)
Previous exposure to anti-TB therapy >30 days	9/12 (75)
Median (IQR) number of times treated with anti-TB drugs >1 month	2 (0.5–8)

Data are presented as n/N (%), unless otherwise stated. IQR: interquartile range.

TABLE 2 Clinical characteristics of 12 patients with multidrug-resistant/extremely drug-resistant tuberculosis (TB) treated with linezolid in Sondalo, Italy

Patient ID	Drug resistance profile	Anti-TB regimen	Sputum smear conversion days	Sputum culture conversion days	Linezolid exposure days	Adverse events
1	H, R, EMB, ETH	AMK, LZD, MFX, PZA, TER	25	47	44	
2	H, R, S, EMB, PZA, FQ, ETH, AMK, KM	AM, CLOF, LEVO, LZD, MRP, TER	54	120	77	Anaemia, leukopenia
3	H, R, S, EMB, PZA, CS	AMK, ETH, LZD, MFX, MRP, PAS	5	No conversion	50	
4	H, R, S, EMB, FQ, ETH, AMK, CM, KM	AM, CLOF, CS, LZD, MFX, MRP, PZA	23	38	110	
5	H, R, PZA, FQ, ETH, PAS, CM	AM/Cl, AMK, CS, ETH, LZD, MFX, MRP	35	No conversion	50	
6	H, R, S, EMB, FQ, ETH, AMK, PAS, CM, KM	AM, CLOF, LZD, MFX, MRP, PZA	74	95	174	
7	H, R, S, EMB, PZA, ETH, PAS, KM	AM, AMK, CLOF, CS, LZD, MFX, MRP	46	70	83	
8	H, R, S, PZA, FQ, ETH, PAS, KM	AM, AMK, CLOF, CS, EMB, LZD, MRP	34	44	90	
9	H, R, S, EMB, PZA, CS, PAS, KM	AM, AMK, ETH, LZD, MRP, TER	22	37	20	Low platelets (LZD temporary interruption)
10	H, R, S, PZA, FQ, PAS	AMK, EMB, ETH, LZD, MFX, TER	52	84	20	Neuropathy (LZD temporary interruption)
11	H, R, S, EMB, PZA, PAS	AM, AMK, ETH, LZD, MFX, MRP	147	No conversion	30	
12	H, R, S, EMB, PZA, FQ, ETH, CS, PAS	AM, AMK, CLOF, ETH, LZD, MFX, MRP, PZA	139	150	120	Neuropathy

AM: amoxicillin; AM/Cl: amoxicillin/clavulanate acid; AMK: amikacin; CLOF: clofazimine; CM: capreomycin; CS: cycloserine; EMB: ethambutol; ETH: ethionamide; FQ: any fluoroquinolone; H: isoniazid; KM: kanamycin; LEVO: levofloxacin; LZD: linezolid; MFX: moxifloxacin; MRP: meropenem; PAS: *p*-aminosalicylic acid; PZA: pyrazinamide; R: rifampicin; S; streptomycin; TER: terizidone.

The features of the Sondalo cohort cases (table 1) are substantially similar to those illustrated by VILLAR *et al.* [1], the prevalence of resistance to first-line anti-TB drugs being similar, the prevalence of resistance to XDR-TB-defining drugs slightly lower and the proportion of previous exposure to anti-TB drugs (as well as the number of previous anti-TB treatment exposures >30 days) slightly higher.

The majority of the cases (11 (91.7%) out of 12) were migrants from high MDR-TB burden countries (six from Romania, two from Ukraine, one from Moldova, one from Pakistan and one from India) *versus* almost one-third (five (31.3%) out of 16; p=0.0014) reported in Portugal [1].

In our cohort, linezolid was administered for a median (interquartile range (IQR)) time of 63.5 (37–100) days with a dosage of 600 mg twice a day for the majority (10 (83.3%) out of 12) of the cases, while two patients were prescribed 600 mg once daily and 450 mg twice a day, respectively.

All patients were males, with a mean±SD age of 40±9.2 yrs. Two cases were HIV infected and were treated with antiretroviral

TABLE 3 Comparison of 12 patients with multidrug-resistant/extremely drug-resistant tuberculosis treated with linezolid in Sondalo with two other recently published cohorts

	Sondalo cohort	MIGLIORI [3]	p-value#	VILLAR [1]	p-value¶
Time to sputum smear conversion days	40.5 (24–64)	76 (56–162)	0.0101	150 (60–540)	0.0028
Time to culture conversion days	70 (44–95)	108 (56–160)	0.1865	180 (90–1380)	0.0197

Data are presented as median (interquartile range), unless otherwise stated. #: comparison between Sondalo and MIGLIORI [3] cohorts; ¶: comparison between Sondalo and VILLAR [1] cohorts.

drugs, while two patients underwent surgery in addition to chemotherapy.

As in other reference centres, the E. Morelli Hospital needs to transfer out all admitted cases to the hospitals referring them for specialised treatment, when culture conversion and clinical stability have been achieved. Patients were transferred out after a median (IQR) hospital stay of 75.5 (51.5–127.5) days; 12 (100%) out of 12 and nine (75%) out of 12 achieved sputum-smear and culture conversion, after a median (IQR) time of 40.5 (24–64) and 70 (44–95) days, respectively. As of June 2011, one patient was cured, two had died and nine were still under treatment.

Four (33.3%) cases reported adverse events, two being major (16.7%; neuropathy and low platelet count, needing temporary interruption of linezolid) and two minor (neuropathy and mild anaemia). All adverse events were reversible.

In conclusion, despite the intrinsic difficulty of evaluating the safety and tolerability of linezolid (administered within different regimens including multiple anti-TB drugs guided by drug susceptibility testing), the study results are consistent with the findings described by VILLAR *et al*. [1] and SCHECTER *et al*. [10]. Based on the results of the study, the dose of linezolid has been reduced in Sondalo from a minimum of 450 to a maximum of 600 mg·day^{-1} (determined by kinetics performed on all cases).

At present, a systematic review including information from the patients treated with linezolid globally is probably the easiest option to better define the efficacy, safety and tolerability of the drug in the treatment of MDR-/XDR-TB.

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Octreotide treatment of idiopathic pulmonary fibrosis: a proof-of-concept study

To the Editors:

Idiopathic pulmonary fibrosis (IPF) is the most frequent form of idiopathic interstitial pneumonia. It is a chronic, progressive and fatal disease of unknown aetiology, characterised by histological features of usual interstitial pneumonia (UIP). Disease progression is marked by worsening dyspnoea, progressive loss of lung volume, abnormal gas exchange and poor quality of life. Median survival after diagnosis is 3–5 yrs. Currently, pirfenidone is the only drug approved in Europe for the treatment in IPF, as it has been shown to slow the decline of lung function [1]. However, no effect on survival has been demonstrated until now.

Somatostatin is an endogenous cyclic peptide initially identified as a regulator of growth hormone secretion. In humans, it has been shown to bind with equal efficiency to five receptors: sst1, sst2A, sst3, sst4 and sst5. We have recently shown that the sst2A receptor is highly expressed in fibrotic lung tissue in IPF patients