Discordant rifampicin susceptibility results are associated with Xpert® MTB/RIF probe B and probe binding delay

R. H. Berhanu,^{*,†‡} K. Schnippel,[§] R. Kularatne,[¶] C. Firnhaber,^{§#} K. R. Jacobson,^{**} C. R. Horsburgh,^{††} C.K. Lippincott^{‡‡}

^{*}Division of Infectious Diseases, University of North Carolina at Chapel Hill, North Carolina, USA; [†]Department of Medicine, Faculty of Health Sciences, Health Economics and Epidemiology Research Office, University of the Witwatersrand, Johannesburg; [‡]Right to Care, Johannesburg; [§]Clinical HIV Research Unit, Department of Medicine, Faculty of Health Sciences, and [¶]National Institute for Communicable Diseases/National Health Laboratory Service and Department of Clinical Microbiology and Infectious Diseases, University of the Witwatersrand, Johannesburg, South Africa; [#]Department of Medicine, Infectious Disease Division, University of Colorado, Denver, Colorado, ^{**}Section of Infectious Diseases, Boston University School of Medicine, Boston, Massachusetts, ^{††}Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts, ^{‡‡}Department of Medicine, Division of Infectious Diseases, Johns Hopkins University, Baltimore, Maryland, USA

SUMMARY

SETTING: Xpert® MTB/RIF is the first-line diagnostic test for *Mycobacterium tuberculosis* and rifampicin (RIF) resistance in South Africa.

OBJECTIVE: To describe the rates of Xpert RIF resistance not confirmed on follow-up testing, as well as the patient and test characteristics associated with discordant results.

DESIGN: Retrospective review of patients with isolates showing Xpert RIF resistance. Line-probe assay, phenotypic drug susceptibility testing or repeat Xpert were all considered confirmatory tests of RIF resistance. ‘Discordance’ was defined as a patient with RIF resistance identified on initial Xpert testing, with a subsequent

confirmatory test indicating RIF susceptibility. Associations were analysed using Pearson χ^2 difference of proportions and modified Poisson regression.

RESULTS: RIF discordance occurred in 22/263 subjects and was associated with Xpert probe B, probe binding delay, as opposed to probe dropout, and probe binding delays (Δ Ct) of between 4 and 4.9.

CONCLUSION: Discordant RIF resistance was common in our cohort and was associated with Xpert probe delay and use of probe B.

KEY WORDS: TB; drug-resistant TB; discordance; rifampicin resistance

TUBERCULOSIS (TB) CONTROL programmes worldwide continue to struggle with diagnosing drug-resistant TB (DR-TB). The World Health Organization (WHO) estimates that only 20% of the 580 000 multidrug-resistant TB (MDR-TB) cases worldwide are successfully diagnosed and treated.¹

Although molecular tests such as the line-probe assay (LPA) and culture with phenotypic drug susceptibility testing (pDST) remain the ‘gold standard’, these tests remain expensive and require specialised reference laboratories. In 2010, the WHO endorsed the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA), a nucleic acid amplification test that can rapidly identify both *Mycobacterium tuberculosis* (MTB) and rifampicin (RIF) resistance with minimal laboratory infrastructure.²

The South African National Department of Health (NDOH) implemented Xpert as the first-line test for TB and RIF resistance in 2011. South Africa is now the biggest user of Xpert worldwide.^{1,3} Individuals

with Xpert RIF resistance are treated with second-line anti-tuberculosis drugs while awaiting LPA confirmation.^{1,3} Due to operational challenges, as many as one third of South African subjects treated for DR-TB receive no confirmatory RIF resistance testing.⁴

We aimed to retrospectively review Xpert RIF resistance and confirmatory resistance testing to determine the subject and test characteristics associated with discordant RIF resistance results in a programmatic setting in Johannesburg, South Africa.

STUDY POPULATION AND METHODS

Consecutive subjects with Xpert RIF resistance referred to an out-patient, decentralised, DR-TB treatment facility at the Helen Joseph Hospital, Johannesburg, between 1 June 2012 and 31 January 2015 were reviewed. Subjects without confirmatory RIF resistance testing were excluded. Subject charac-

teristics collected include sex, age, human immunodeficiency virus (HIV) status and CD4 count.

All laboratory tests were performed by the National Health Laboratory Service. Xpert G4 cartridges were used. In accordance with the NDOH diagnostic algorithm, subjects with Xpert RIF resistance provided a second specimen for smear microscopy, GenoType MTBDR_{plus} LPA (Hain Lifescience, Nehren, Germany) and mycobacterial culture.³ Culture and pDST were performed in MGIT[™] (Mycobacterium Growth Indicator Tubes; BD, Sparks, MD, USA) tubes.

The Xpert cycle threshold (C_T) for each *rpoB* molecular beacon probe (A–E) was abstracted. Xpert reports on MTB quantity were categorised as ‘high’ (median $C_T \leq 16$), ‘medium’ ($16 < C_T \leq 22$), ‘low’ ($22 < C_T \leq 28$) and ‘very low’ ($C_T > 28$). Delta C_T (ΔC_T) max was calculated as the difference between the earliest and latest C_T across the five probes. For RIF resistance, the hybridisation pattern of the probes was classified as ‘dropout’ (no hybridisation) or ‘delayed’ ($\Delta C_T > 4$). Resistant ΔC_T values were categorised as ΔC_T 4.1–4.9 vs. $\Delta C_T \geq 5$. The dropout probe or the probe with the most delayed binding C_T was categorised as the ‘resistant’ probe in each case.

‘Discordance’ was defined as an initial Xpert result with RIF resistance with only RIF-susceptible follow-up tests (i.e., any repeat Xpert, LPA or pDST). ‘Heteroresistance’ was defined as an initial Xpert with RIF resistance and both susceptible and resistant follow-up testing, suggesting a mixed infection in the same subject. Heteroresistant subjects were not considered discordant in this analysis.

All analysis was performed using Stata v 14 (StataCorp, College Station, TX, USA). Standard descriptive statistics are presented. Pearson χ^2 was used for proportion differences and Wilcoxon rank-sum (Mann-Whitney) was used for differences in medians. Modified Poisson regression with robust standard errors was used to analyse the relative risk (incidence risk ratio [IRR] of discordance by subject or specimen characteristic) of discordant Xpert RIF results. Unadjusted IRRs with 95% confidence intervals (CIs) are presented for subject characteristics and Xpert test characteristics associated with discordance.

Ethics approval was received from the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg, South Africa.

RESULTS

Of 263 subjects, 124 (47.2%) were male and 213 (81%) were HIV-infected with a median CD4 count of 150 cells/mm³ (interquartile range [IQR] 25–169) (Table 1). The median age was 36 years (IQR 29–42). Pulmonary TB occurred in 245 (93%), 162 of whom (61.6%) were sputum smear-positive. The majority (n

= 189, 71.9%) had no previous TB history, nearly a quarter (n = 62, 23.8%) had been treated previously with first-line anti-tuberculosis medications and a few (n = 12, 4.6%) had been treated previously with second-line medications for MDR-TB.

RIF resistance was confirmed in 241/263 (91.6%) subjects, 15 of whom (6.2%) had evidence of heteroresistance (Table 2). Of those with discordance (22/263, 8.4%), all had ≥ 1 confirmatory LPA demonstrating only RIF susceptibility and 14/22 subjects ≥ 1 repeat Xpert that yielded a RIF-susceptible result. pDST was available for one subject with discordance who was RIF-susceptible. Among those without discordance (n = 226), 50 had ≥ 1 repeat Xpert tests performed (range 0–7 tests, median 1 test), 203 had confirmatory LPA (range 0–7, median 1) and 89 had pDST (range 0–4, median 0).

Xpert probe-binding patterns and C_T value reports were available for 173 subjects (65.8%). Overall Xpert probe dropout (137/173, 79.2%) occurred more commonly than probe delay (36/173, 20.8%) as the indication of resistance; however, probe delay was more common in subjects with discordance (16/22, 87.1%). Although the most common probes for RIF resistance detection were E (n = 64, 37%) and D (n = 59, 34.1%), discordant results were more frequent among probes B (n = 11, 61.1%) and E (n = 4, 22.2%).

In our regression analysis, HIV status, age, sex, previous TB history, positive smear microscopy and Xpert probe quantification were not associated with having a discordant result. Xpert probe delay was strongly associated with discordance (IRR 30.4, 95%CI 7.30–126.90) when compared with probe dropout. Of the 35 subjects with probe delay, ΔC_T 4–4.9 had a greater association with discordance than $\Delta C_T \geq 5$ (IRR 4.09, 95%CI 1.39–12.9). Compared with probe E (the probe most commonly associated with resistance), there was an increased risk of discordance if resistance was detected in probe B (IRR 5.67, 95%CI 1.95–16.45). Discordance with ‘very low’ Xpert results did not achieve statistical significance (IRR 1.22, 95%CI 0.4–3.70).

DISCUSSION

Among patients in Johannesburg diagnosed with RIF-resistant TB on Xpert, we found nearly 1 in 10 subjects had discordant molecular results. Discordant RIF resistance was associated with Xpert probe B, probe binding delay compared with dropout and delays between ΔC_T 4–4.9. pDST was only available in one subject with discordance and demonstrated RIF phenotypic susceptibility. These findings alone did not permit us to determine whether discordance represented false-positive resistance, including silent mutations, heteroresistance or another cause; however, previous Xpert ΔC_T cut-off changes suggest

Table 1 Patient and Xpert® MTB/RIF test characteristics in patients with RR-TB, either confirmed or with discordance and unadjusted predictors of discordance

	All RR-TB patients n/N (%)	Confirmed RIF resistance* n/N (%)	Discordant RIF resistance [†] n/N (%)	Predictors of discordance IRR (95%CI)
Patient characteristics	(n = 263)	241 (91.6)	22 (8.4)	
Male	124 (47.2)	115 (47.7)	9 (40.91)	0.77 (0.34–1.76)
Age, years, median [IQR]	36 [29–42]	36 [29–42]	37 [27–44]	—
HIV-positive (n = 261)	213 (81.7)	198 (82.8)	15 (68.2)	0.48 (0.21–1.07)
CD4 count, cells/mm ³ median [IQR] (n = 173)	150 [25–169]	146 [25–164]	189 [42–348]	—
CD4 <100, cells/mm ³	98/173 (56.7)	91/161 (56.5)	6/12 (50)	1.07 (0.35–3.25)
Previous first-line anti-tuberculosis treatment	62 (23.7)	54 (22.6)	8 (36.4)	1.83 (0.81–4.17)
Previous second-line anti-tuberculosis treatment	12 (4.6)	12 (5)	0	—
Pulmonary TB	245 (93.2)	223 (92.5)	22 (100)	—
Smear-positive	162 (61.6)	148 (61.4)	14 (63.6)	1.09 (0.47–2.51)
Xpert test characteristics [‡]	(n = 173)	(n = 154)	(n = 19)	
Quantitative result				
Very low	25 (14.5)	21 (13.6)	4 (22.2)	1.22 (0.40–3.70)
Low	49 (28.3)	46 (29.7)	3 (16.7)	0.47 (0.13–1.67)
Medium	61 (35.3)	53 (34.2)	8 (44.4)	Referent
High	38 (22)	35 (22.6)	3 (16.7)	0.60 (0.17–2.13)
RIF resistance detection				
Probe dropout	137 (79.2)	135 (87.6)	2 (10.5)	Referent
Probe delay $\Delta C_T > 4$ ^{§¶}	36 (20.8)	19 (12.3)	17 (89.5)	32.2 (7.83–133.62)
Resistance probe				
Probe A	11 (6.4)	10 (6.5)	1 (5.3)	1.45 (0.18–11.82)
Probe B [¶]	31 (17.9)	20 (12.9)	11 (61.1)	5.67 (19.5–16.45)
Probe C	5 (2.9)	5 (3.2)	0	—
Probe D	59 (34.1)	57 (36.8)	2 (11.1)	0.54 (0.10–2.87)
Probe E	64 (37)	60 (38.7)	4 (22.2)	Referent
Multiple probes (A, B, D or B, D or D, E)	3 (1.7)	3 (2)	0	—
ΔC_T in probe delay (n = 35)	(n = 35)	(n = 19)	(n = 16)	
ΔC_T 4–4.9 [¶]	18 (51.4)	5 (26.3)	13 (81.2)	4.09 (1.39–12.07)
$\Delta C_T \geq 5$	17 (47.6)	14 (73.6)	3 (18.8)	Referent
ΔC_T , median [IQR]	6.1 [4.4–7.6]	7.3 [4.7–9.1]	4.6 [4.3–4.8]	—

* Has ≥ 1 test confirming RIF resistance, i.e., second Xpert, LPA or pDST.

[†] 'Discordance' defined as no repeat test confirming RIF resistance with ≥ 1 tests with discordant RIF results (i.e., repeat Xpert, LPA discordance or pDST).

[‡] Xpert probe-binding characteristics only available for a subset of cohort (n = 173).

[§] Delayed binding of an Xpert probe with $\Delta C_T > 4$ (cut-off for resistance in the Generation 4 cartridge).

[¶] Statistically significant.

RR-TB = RIF-resistant tuberculosis; RIF = rifampicin; IRR = incidence risk ratio; CI = confidence interval; IQR = interquartile range; HIV = human immunodeficiency virus; ΔC_T = difference between the maximum and minimum probe C_T values; pDST = phenotypic drug susceptibility testing, LPA = line-probe assay; CT = cycle threshold.

false-positive results occurring around the ΔC_T cut-off are a plausible explanation.

False-positive RIF resistance due to the ΔC_T cut-off was noted in earlier Xpert assay generations.² In 2010, the ΔC_T for determination of RIF resistance was increased from 3.5 to 5 (G2 and G3 assay versions), and then later adjusted to 4 in the G4 assay.² The high rate of discordance in our cohort thus occurred mostly with probe delay close to the RIF resistance determination cut-off limit of the current G4 cartridge (ΔC_T 4–4.9). This finding has yet to be reported in other settings, but may reflect an indeterminate range. Discordance with 'very low' Xpert MTB quantity has been reported in Cape Town, South Africa, and Haiti,^{5,6} but did not reach statistical significance in our study.

The majority of RIF resistance discordance between molecular and pDST is related to clinically significant resistance that is not detected using current MGIT pDST methods.^{7,8} In these cases, the molecular test is felt to be correct. However, these mutations are detected using all molecular tests

(Xpert and LPA) and would not explain the Xpert vs. LPA molecular discordance we identified in our study. There are rare (<1%) cases of silent *rpoB* mutations detected using Xpert that do not confer clinically relevant resistance and are considered as false-positive molecular testing.⁸ Conversely, false-negative Xpert RIF susceptibility results can occur with heteroresistance if <90% of the populations in a specimen are RIF-resistant^{9,10} or in the presence of mutations outside of the RIF resistance-determining region (RRDR) such as *rpoB* I491F¹¹, and the L533P mutation (within the RRDR) that is suboptimally identified using Xpert.¹² Our findings of Xpert resistance not confirmed using LPA or repeat Xpert suggest complexities of the current technology that warrant additional research.

The present study had important limitations. As pDST for RIF is not the standard of care, results were only available for a single patient with discordance, so phenotypic expression of much of the discordance was lacking. Even without this information, the high rate of non-agreement between molecular tests

Table 2 Xpert® MTB/RIF, LPA and pDST RIF susceptibility results for patients with discordance or heteroresistant infection

Patient	Xpert RIF-resistant results	Xpert RIF-susceptible results	RIF-resistant results on LPA*	RIF-susceptible results on LPA*	RIF-resistant results on pDST	RIF-susceptible results on pDST	Interpretation
1	1	0	0	1	0	0	Discordant [†]
2	1	0	0	1	0	0	Discordant
3	1	0	0	1	0	0	Discordant
4	1	0	0	2	0	0	Discordant
5	1	1	0	1	0	0	Discordant
6	1	0	0	2	0	0	Discordant
7	1	0	0	1	0	0	Discordant
8	1	1	0	1	0	0	Discordant
9	1	3	0	3	0	0	Discordant
10	1	1	0	2	0	0	Discordant
11	1	1	0	1	0	0	Discordant
12	1	2	0	2	0	0	Discordant
13	1	4	0	5	0	1	Discordant
14	1	1	0	3	0	0	Discordant
15	1	3	0	2	0	0	Discordant
16	1	2	0	1	0	0	Discordant
17	1	0	0	1	0	0	Discordant
18	1	0	0	2	0	0	Discordant
19	1	3	0	2	0	0	Discordant
20	1	1	0	3	0	0	Discordant
21	1	3	0	3	0	0	Discordant
22	1	3	0	2	0	0	Discordant
23	1	0	1	1	0	0	Heteroresistant [‡]
24	1	0	2	1	0	1	Heteroresistant
25	5	1	0	1	0	0	Heteroresistant
26	2	2	0	3	0	1	Heteroresistant
27	2	0	3	1	0	0	Heteroresistant
28	2	1	1	3	0	0	Heteroresistant
29	1	1	1	1	0	0	Heteroresistant
30	1	1	0	1	1	1	Heteroresistant
31	1	1	0	2	1	1	Heteroresistant
32	1	1	1	2	0	1	Heteroresistant
33	1	1	3	0	1	0	Heteroresistant
34	1	1	3	0	0	0	Heteroresistant
35	5	1	9	1	1	0	Heteroresistant
36	1	0	1	1	1	0	Heteroresistant
37	1	2	6	0	0	0	Heteroresistant

* GenoType® MTBDRplus LPA, Hain Lifescience, Nehren, Germany.

[†] Defined as an initial Xpert with RIF resistance with ≥ 1 follow-up RIF-susceptible tests (i.e., Xpert, LPA or pDST) and no repeat test confirming RIF resistance.

[‡] Defined as an initial Xpert result with RIF resistance, with ≥ 1 follow-up RIF-resistant test along with ≥ 1 follow-up RIF-susceptible result.

LPA = line-probe assay; pDST = phenotypic drug susceptibility testing; RIF = rifampicin.

indicate further investigation to the cause of discordance is needed. Targeted deep sequencing of discordant isolates would allow for an understanding of within-specimen genetic variability and provide guidance on how to interpret these cases. However, such sequencing was not routinely available in the study setting.

CONCLUSION

Discordant RIF resistance has significant clinical implications, including, at best, anxiety for patients and health care workers and, at worst, incorrect medical decision-making leading to unnecessary toxic, prolonged and costly treatment. Due to the high stakes of misdiagnosing RIF resistance, clinicians in high DR-TB burden settings should be aware of the association between RIF resistance discordance and probe-binding delay on the Xpert G4 cartridge described in our study, and 'very low' quantity of MTB seen in other settings.^{5,6} Patients with discor-

dance should have multiple repeat susceptibility tests performed using various methods, including molecular, pDST and sequencing, to rule out false-positive RIF resistance detection.

Acknowledgements

The authors thank the staff of the TB focal point clinic at Helen Joseph Hospital, Johannesburg, South Africa, particularly P Baloyi and N Mthupha, for their assistance.

This study was supported by the United States Agency for International Development, Washington DC, USA (Innovations Research on HIV/AIDS, grant number USAID-674-A-12-00029); and the National Institute of Health Fogarty International Center, Bethesda, MD, USA (grant number D43TW009340 to RB). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of interest: RB has received funding for domestic conference attendance from Cepheid (Sunnyvale, CA, USA).

References

- 1 World Health Organization. Global tuberculosis report, 2016. WHO/HTM/TB/2016.13. Geneva, Switzerland: WHO, 2016.

- 2 Steingart K, Schiller I, Horne D, et al. Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev* 2014; 1: CD009593.
- 3 National Department of Health Republic of South Africa. South African national tuberculosis management guidelines. Pretoria, South Africa: NDoH, 2011.
- 4 Churchyard G, Mametja L, Mvusi L, et al. Tuberculosis control in South Africa: successes, challenges and recommendations. *South African Med J* 2014; 104: 1–3.
- 5 Beylis N C, Ghebrekristos Y, Wojno J, Nicol M, Simpson J, Da Silva P. Characterization of *Mycobacterium tuberculosis* complex isolates with discordant rifampicin susceptibility test results. [Abstract EP-141-04]. 46th World Conference on Lung Health, Cape Town, South Africa. *Int J Tuberc Lung Dis* 2015; 19 (Suppl 2): S105.
- 6 Ocheretina O, Byrt E, Mabou M, et al. False-positive rifampin resistant results with Xpert MTB/RIF version 4 assay in clinical samples with a low bacterial load. *Diagn Microbiol Infect Dis* 2016; 85: 53–55.
- 7 Van Deun A, Aung K, Bola V, et al. Rifampin drug resistance tests for tuberculosis: challenging the gold standard. *J Clin Microbiol* 2013; 51: 2633–2640.
- 8 Hofmann-Thiel S, Hoffmann H, Hillemann D, Rigouts L, Deun Van A, Kranzer K. How should discordance between molecular and growth-based assays for rifampicin resistance be investigated? *Int J Tuberc Lung Dis* 2017; 21: 721–726.
- 9 Blakemore R, Story E, Helb D, et al. Evaluation of the analytical performance of the Xpert MTB/RIF assay. *J Clin Microbiol* 2010; 48: 2495–2501.
- 10 Zetola N M, Shin S S, Tumedi K A, et al. Mixed *Mycobacterium tuberculosis* complex infections and false-negative results for rifampin resistance by GeneXpert MTB/RIF are associated with poor clinical outcomes. *J Clin Microbiol* 2014; 52: 2422–2429.
- 11 Sanchez-Padilla E, Merker M, Beckert P, et al. Detection of drug-resistant tuberculosis by Xpert MTB/RIF in Swaziland. *N Engl J Med* 2015; 372: 1181–1182.
- 12 Rufai S B, Kumar P, Singh A, Prajapati S, Balooni V, Singh S. Comparison of Xpert MTB/RIF with line-probe assay for detection of rifampin-mono-resistant *Mycobacterium tuberculosis*. *J Clin Microbiol* 2014; 52: 1846–1852.

R É S U M É

CONTEXTE : L'Xpert® MTB/RIF est le test diagnostique de première ligne pour *Mycobacterium tuberculosis* et pour la résistance à la rifampicine (RIF) en Afrique du Sud.

OBJECTIF : Décrire les taux de résistance à la RIF par Xpert qui n'ont pas été confirmés lors des tests de suivi ainsi que les caractéristiques du patient et du test associées à ces résultats discordants.

SCHEMA : Revue rétrospective des patients ayant des isolats montrant une résistance à la RIF par Xpert. Le test de sonde en ligne, le test de pharmacosensibilité phénotypique ou la répétition de l'Xpert ont tous été considérés comme des tests de confirmation de la résistance à la RIF. La discordance a été définie comme

une résistance à la RIF identifiée lors de l'Xpert initial avec un test de confirmation ultérieur indiquant une sensibilité à la RIF. Les associations analysées grâce à la différence de proportion de Pearson χ^2 et à la régression modifiée de Poisson.

RÉSULTATS : Une discordance relative à la RIF est survenue chez 22/263 sujets et a été associée avec l'Xpert sonde B, retard plutôt que l'absence de fixation de la sonde, et des retards entre ΔCt 4–4,9.

CONCLUSION : Une discordance relative à la résistance à la RIF a été fréquente dans notre cohorte et associée avec un retard d'hybridation de la sonde Xpert et avec la sonde B.

R E S U M E N

MARCO DE REFERENCIA: La prueba Xpert® MTB/RIF es el método preferido de diagnóstico del *Mycobacterium tuberculosis* y la resistencia a rifampicina (RIF) en Suráfrica.

OBJETIVO: Describir las tasas de resistencia a RIF detectada con la prueba Xpert, que no se confirmó con las pruebas de seguimiento y las características de los pacientes que se asociaron con estos resultados discordantes.

MÉTODO: Se practicó un análisis retrospectivo de los pacientes con aislados que habían revelado resistencia a RIF con la prueba Xpert. Se consideraron como pruebas confirmatorias de la resistencia las pruebas con sondas en línea, las pruebas fenotípicas de sensibilidad a los medicamentos o la repetición de la prueba Xpert. Se definió la discordancia como un paciente con resistencia

a RIF en la prueba Xpert inicial, cuyas pruebas confirmatorias posteriores revelaron sensibilidad a RIF. Al analizar las asociaciones se utilizó la prueba χ^2 de Pearson para las diferencias de proporciones y la regresión de Poisson modificada.

RESULTADOS: Se observó discordancia con respecto a la resistencia a RIF en 22 de 263 personas; la discordancia se asoció con la sonda B de la prueba Xpert, un retraso de hibridación de la sonda más que una ausencia de hibridación, y retrasos con respecto al umbral ΔCt de 4 a 4,9.

CONCLUSION: La discordancia con respecto a la resistencia a RIF fue frecuente en la cohorte estudiada y se asoció con un retraso en la fijación de la sonda B en la prueba Xpert.