

patients underwent portosystemic shunt, one underwent liver transplantation, and another died after 12 years. All were on continuous anticoagulation therapy.

Among eight patients with EHPVT and MPD (5 male, mean age 55 years), five had ET, two had PMF and one had PRV. On admission, all had signs of portal hypertension and five experienced superior mesenteric vein thrombosis. They are all alive after a mean period of 1.8 years (range, 0.2–6 years) of observation. All patients have been receiving continuous anticoagulation therapy.

Non-cirrhotic portal hypertension is an under-recognised entity that closely mimics cirrhosis and needs a strong index of suspicion for the diagnosis. JAK2V617F mutation is found in nearly all cases of PRV and about half the cases of ET and PMF.⁵ However, JAK2V617F was present in all patients assessed for the mutation, including those with ET and PMF, a finding reported recently also by other investigators.⁴ The ubiquitous presence of JAK2V617F may express a more aggressive phenotype with an increased risk of thrombosis at these distinct sites.

In conclusion, JAK2V617F assessment has a unique role in early diagnosis and consequently management of myeloproliferative disorders in the presence of splanchnic vein thrombosis.

ACKNOWLEDGEMENT

Declaration of personal and funding interests: None.

REFERENCES

1. Landolfi R, Di Gennaro L, Falanga A. Thrombosis in myeloproliferative disorders: pathogenetic facts and speculation. *Leukemia* 2008; **22**: 2020–8.
2. Smalberg J, Kruip MHHA, Janssen HLA, Rijken DC, Leebeek FWG, Maat MPM. Hypocoagulability and hypofibrinolysis and risk of deep vein thrombosis: similarities and differences. *Arterioscler Thomb Vasc Biol* 2011; **31**: 485–93.
3. Bayraktar Y, Harmanci O, Büyükasik Y, *et al.* JAK2V617F mutation in patients with portal vein thrombosis. *Dig Dis Sci* 2008; **53**: 2778–83.
4. Orr DW, Patel RK, Lea NC, *et al.* The prevalence of the activating JAK2 tyrosine kinase mutation in chronic porto-spleno-mesenteric venous thrombosis. *Aliment Pharmacol Ther* 2010; **31**: 1330–6.
5. Tefferi A, Skoda R, Vardiman JW. Myeloproliferative neoplasms: contemporary diagnosis using histology and genetics. *Nat Rev Clin Oncol* 2009; **6**: 627–37.

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doi:10.1111/j.1365-2036.2011.04672.x

First-line treatments for hepatitis C

SIRS, Although sustained virological response (SVR) is only a surrogate endpoint, the meta-analysis by Brok *et al.*¹ shows that, in the treatment of naive patients, the combination of interferon and ribavirin improves the rate of SVR as compared with interferon alone (event rate ratio: 1.39; 95% confidence interval: 1.32 to 1.47). For this clinical indication, protease inhibitors are thought to be a further advancement,² and both telaprevir and boceprevir have already been assessed in phase III trials. Boceprevir is supported by a full paper;³ the full report for telaprevir is not yet available, but extensive information has already been published.⁴

In its simplest form,⁵ network meta-analysis⁶ can be useful to summarise therapeutic problems, wherein new agents show promising data, but head-to-head

comparisons are lacking. As treatments for naive patients with hepatitis C fall in this area, we have carried out a simplified analysis to better interpret the information presently available.

In evaluating interferon and ribavirin (IR) alone or in combination with either agent (T12 = telaprevir given for 12 weeks; B48 = boceprevir given for 48 weeks), the addition of a protease inhibitor significantly improved the rates of SVR (event rate ratio = 1.70 for T12IR and 1.75 for B48IR). Figure 1, which has been generated according to a simplified graphical technique of network meta-analysis,⁵ summarises the comparative effectiveness of interferon alone, IR, T12IR and B48IR. Direct comparisons represent 'real' clinical trials, whereas the indirect ones are the result of statistical indirect inference.

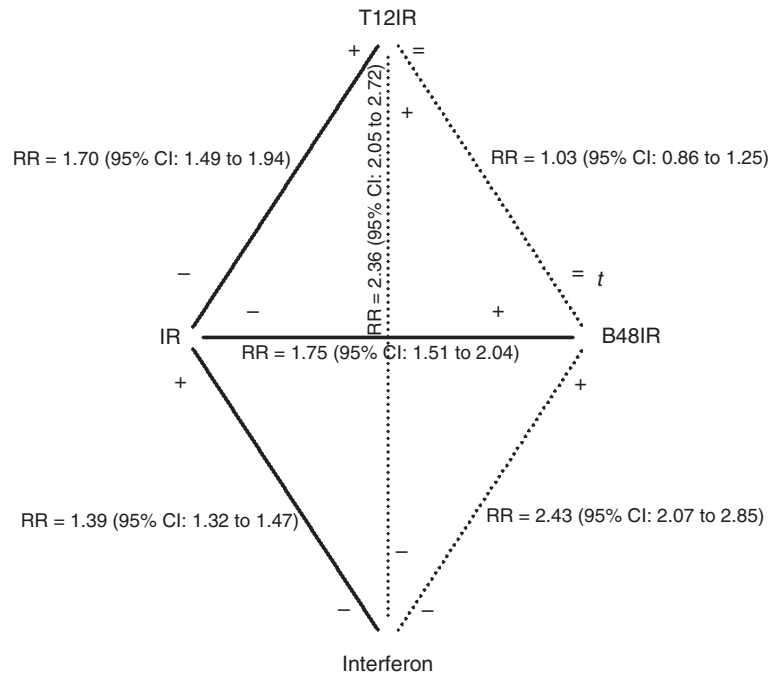


Figure 1 | Network meta-analysis of first-line treatments for hepatitis C. The graph summarises the results of both direct and indirect comparisons between treatments for naive patients. Each direct comparison is represented by a solid line and each indirect comparison by a dotted line. The endpoint is the proportion of patients achieving SVR; no differentiation is made between interferon and pegylated interferon. Statistical results of event rate ratio are presented as relative risk (RR) with 95% confidence interval (CI). The RR value reported by Brok *et al.*¹ for no achievement of SVR has been rearranged to express the achievement of SVR. Symbols: '+' indicates which treatment is favoured at levels of statistical significance, and viceversa for '-'; '=' denotes comparisons showing no significant difference; 't' indicates which treatment is favoured by a trend in cases of no significant difference. The clinical trials on the two protease inhibitors also evaluated adjunctive telaprevir given for 8 weeks and adjunctive boceprevir given for 24 weeks, which have not been included in the graph, but can be examined in the Supporting Information material posted on the web (Figure S1). SVR, sustained virological response; IR, interferon+ribavirin; T12IR, IR in combination with telaprevir given for 12 weeks; B48, IR in combination with boceprevir given for 48 weeks (see Ref. 4 for further details).

The overall picture of the comparisons shown in Figure 1 indicates that protease inhibitors can determine a significant improvement in SVR in comparison with older agents. Hence, our results extend the effectiveness data presented by Brok *et al.*,¹ and in addition show that a simplified network meta-analysis graph can effectively summarise all therapeutic information contrasting newer with older treatments.

ACKNOWLEDGEMENTS

Declaration of personal interests: None. *Declaration of funding interests:* One of the authors (DM) was supported by a grant from the Italian Society of Hospital Pharmacists.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Network meta-analysis of first-line treatments for hepatitis C.

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REFERENCES

1. Brok J, Gluud LL, Gluud C. Meta-analysis: ribavirin plus interferon vs. interferon monotherapy for chronic hepatitis C – an updated Cochrane review. *Aliment Pharmacol Ther* 2010; **32**: 840–50.
2. Cholongitas E, Papatheodoridis GV. Novel therapeutic options for chronic hepatitis C. *Aliment Pharmacol Ther* 2008; **27**: 866–84.
3. Poordad F, McCone J Jr, Bacon BR, *et al.* Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* 2011; **364**: 1195–206.
4. Pawlotsky JM. The results of phase III clinical trials with telaprevir and boceprevir presented at the liver meeting. *Gastroenterology* 2011; **140**: 746–54.
5. Fadda V, Maratea D, Trippoli S, Messori A. Network meta-analysis. Results can be summarised in a simple figure. *BMJ* 2011; **342**: d1555.
6. Caldwell DM, Ades AE, Higgins JPT. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005; **331**: 897–900.