

WITN3298 **037**

Central Manchester and Manchester
Children's University Hospitals



NHS Trust

Dr CRM Hay - Haemophilia Centre Director
Consultant Haematologist

Miss K Jones
Secretary to Dr CRM Hay

Telephone: +44 (0)

Facsimile: +44 (0)

E-mail:

GRO-C

GRO-C

Our ref: CRMH/KJ/clinics/outpatients/2002/crmh/march 14/M63/01420

21 March 2002

Clinic Visit: 14th March 2002

Professor TW Warnes
The Liver Clinic
Manchester Royal Infirmary

26/3/02
Notes & record
reply
+ run

Dear Tom

Mr Paul Bullen DoB: GRO-C 1958

GRO-C

Diagnosis: Moderate Haemophilia
Hepatitis C
Cirrhosis

I saw Paul in clinic this morning, shortly after he had been seen in the Liver Clinic. I gather, from Paul, that your team agree that he should be considered, or at least listed, in the transplant program. I understand that he has been genotyped. I do not know whether his Hepatitis C viral load has been determined. It may be worth considering pegylated Interferon and Ribavirin, particularly if his genotype turns out to be a non-type 1. About 2/3 of our patients turn out to be one of the sub-types of type 1. The remainder have all sorts of genotypes, including two who are type 5. His likelihood of responding if he turns out to be type 1 and has cirrhosis would be very low. My other concern is that he is one of the small proportion of patients with Hepatitis C who have a chronic fatigue syndrome. My very limited experience of treating such patients has been that their chronic fatigue syndrome got considerably worse and they were unable to tolerate treatment. This experience is so limited however that I would not deny him treatment on that basis. At the end of the day, if he finds the treatment intolerable he can always stop it. I would be very interested to hear from you what you have found in that situation. In anticipation that he may, or may not go ahead with Interferon and Ribavirin treatment, I will make the administrative moves to obtain funding. There is, after all, not obligation for him to take this up.

He seems generally well. His albumen is 35, Hb 14.6g/dl and he is going to continue taking oral iron for about another month. I note his GP checked his ferritin but in someone with severe liver disease this will be uninformative. We will review him in a couple of months when he comes back to the liver clinic.

Yours sincerely

GRO-C

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Dr MW Mason
The Kiltearn Medical Centre
Hospital Street
Nantwich
Cheshire CW5 5RL

PS - I have discussed the treatment side effects with him at length.



Incorporating:
Royal Manchester Children's Hospital ♦ Manchester Royal Infirmary ♦ Manchester Royal Eye Hospital
Booth Hall Children's Hospital ♦ Saint Mary's Hospital for Women and Children ♦ University Dental Hospital of Manchester



memo

Paul BULLEN - 63/1420



Ali,

Could we discuss this patient? Please see enclosed letter from Dr. Hay. As I understand it, Paul Bullen has moderately severe haemophilia and insulin requiring diabetes mellitus. He has oesophageal varices and has previously had a peptic ulcer as well as a hyperplastic polyp in the gastric antrum, which was removed by polypectomy; I am not clear whether this procedure was covered by Factor VIII. He had a melaena in October 1999 requiring a 4 unit blood transfusion. Liver biopsy in November 1995 at the time of laparoscopic cholecystectomy showed chronic hepatitis with fibrosis. He is said to have cirrhosis. I am not sure where this impression comes from; has cirrhosis ever been documented histologically? The liver biopsy was followed by an intra-abdominal bleed requiring further laparotomy but the source of the bleed was not determined. Please chase up for me the result of the liver biopsy, together with his recent genotype and we could then discuss the case together before I reply to Dr. Hay.

TWW 9/4/02.

Liver biopsy was done Nov 95 and showed severe fibrosis not amounting to cirrhosis (I will ask Ray to comment on the histology during our next meeting)

his genotype B

GRO-C: Dr A
Aboutwerat



Awarded for excellence

DEPARTMENT OF GASTROENTEROLOGY

Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

Telephone: Fax: Email: twwarnes

Our ref AA/PSH/M63/01420
NHS No 4523073333

Typed 24 April 02

Dr R McMahon
Consultant Histopathologist
MRI

OPA
23/5
T. J. WILKINSON

Dear Raymond

Re: **Mr Paul BULLEN - DOB** **1958**

I would be grateful if you could review the biopsy of Mr Bullen, No. P9505604/S dated 2nd November 1995, arranged by Mr Mr Bullen is a patient with known haemophilia, chronic hepatitis C and he had this liver biopsy intra-operatively. He is being considered for antiviral treatment for hepatitis C.

Yours sincerely

Dr A Aboutwerat
Clinical Research Fellow

Dr CRM Hay – Haemophilia Centre Director
Consultant Haematologist

Miss K Jones
Secretary to Dr CRM Hay

Telephone: +44 (0) [GRO-C]

Facsimile: +44 (0) [GRO-C]

E-mail: [GRO-C]

Our ref: CRMH/KJ/clinics/outpatients/2002/crmh/may 23/M63/01420

Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology
Cobbett House (Orange Zone)
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

NHS No.: 452 307 3333

27 May 2002

Clinic Visit: May 23 2002

Dr MW Mason
The Kiltearn Medical Centre
Hospital Street
Nantwich
Cheshire CW5 5RL

Dear Dr Mason

Mr Paul Bullen DoB: [GRO-C] 1958

[GRO-C]

Diagnosis: Severe Haemophilia
Portal Hypertension
Diabetes Mellitus
Hepatitis C

Paul was reviewed today by us and by the Liver Clinic. We have both been discussing possible treatment for his Hepatitis C for sometime. Paul is hepatitis C genotype III, overall this has an 80% response rate to pegylated Interferon and Ribavirin, however Paul's pre-existing cirrhosis clearly reduces likelihood of responding considerably. Nevertheless, he may derive useful palliation from this treatment and I think both the Hepatologists and ourselves feel that this would be worthwhile. I have spent quite a long time today discussing the potential side effects with Paul and his wife. These side effects are all extremely common and include malaise, lethargy, depression, tetchiness, thrombocytopenia and autoimmune haemolytic anaemia and neutropenia. Paul has a post viral fatigue syndrome. My limited experience in treating such patients with Interferon is that this tends to get worse, but I have told him that I think this is unpredictable. He has suffered from depression and is on 10mg of Amitriptyline a day. He was unable to tolerate a higher dose but finds that 10mg a day helps his spleen pattern. Should he become depressed we would have to consider changing this to a different drug. The treatment may effect his insulin requirements and he knows to keep a close eye on his blood sugar when he starts. He is already thrombocytopenic, secondary to portal hypertension and this may well get worse when he starts treatment. We would hold fast with the dosage until the platelet count had fallen below $30 \times 10^9/l$. It would be helpful if we could arrange joint monitoring with Dr Patterson at Leighton Hospital in Crewe. We have made this arrangement for other patients living in South Cheshire in the past and it has worked very well. This would minimise his need to visit us up here since we will need to keep a very close eye on his blood count.

Continued.....

*Dr CRM Hay – Haemophilia Centre Director
Consultant Haematologist*

Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology
Cobbett House (Orange Zone)
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

Miss K Jones
Secretary to Dr CRM Hay

Telephone: +44 (0) [GRO-C]

Facsimile: +44 (0) [GRO-C]

E-mail: [GRO-C]

Our ref: CRMH/KJ/clinics/outpatients/2002/crmh/may 23/M63/01420

NHS No.: 452 307 3333

27 May 2002

Clinic Visit: May 23 2002

Continued.....

Mr Paul Bullen DoB: [GRO-C] 1958

[GRO-C]

Diagnosis: Severe Haemophilia
Portal Hypertension
Diabetes Mellitus
Hepatitis C

I expect him to be admitted under the Hepatologists to start treatment very shortly. We do most of the monitoring and the Interferon will be paid for through our contractual structure.

Yours sincerely

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Professor TW Warnes
Consultant Gastroenterologist
Dept of Gastroenterology
Manchester Royal Infirmary

Diabetic Department
Leighton Hospital
Middlewich Road
Leighton
Crewe

Dr M Patterson
Dept of Haematology
Leighton Hospital
Middlewich Road
Leighton
Crewe

DEPARTMENT OF GASTROENTEROLOGY

Manchester Royal Infirmary,
Oxford Road,
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C**

Fax: **GRO-C**

email: twwarnes@**GRO-C**

Our ref AA/JMH/M63/01420
NHS No 4523073333

Liver Clinic: 23 May 02

Dr M W Mason
The Kiltearn Medical Centre
Hospital Street
Nantwich
CW5 5RL

27 May 2002

Dear Dr Mason

Re: Mr Paul BULLEN - DOB: **GRO-C 1958**

GRO-C

I reviewed this man on 23.5.02. He is keeping well and has agreed to commence treatment with Interferon and Ribavirin for chronic hepatitis C and I have made arrangements for him to be admitted on 5 June to commence Viraferon peg 50 µgm a week and Ribavirin 1 gm a day, in two divided doses. We will monitor his FBC and LFT's throughout treatment.

I have repeated his blood tests and we will review him in clinic the week after treatment is commenced.

Yours sincerely,

DR. A. ABOUTWERAT
Clinical Research Fellow

DEPARTMENT OF GASTROENTEROLOGY

Manchester Royal Infirmary

Oxford Road

MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C**

Fax: **GRO-C**

email: twwarnes@**GRO-C**

Our ref AA/JMH/M63/01420
NHS No 4523073333

Liver Clinic: 19 June 02

Dr M W Mason
The Kiltearn Med Centre
Hospital Street
Nantwich
CW5 5RL

24 June 2002

Dear Dr Mason

Re: Mr Paul BULLEN – DOB **GRO-C 1958**

GRO-C

Diagnosis; Moderate haemophilia.
Chronic hepatitis C, genotype 3 on Viraferon peg 50 µgm week and Ribavirin 600 mg a day.

I reviewed this man on 19.6.02. He tolerates treatment well with a WCC of 2.2, Hb 13.9, platelets 49, neutrophils 0.98 and lymphocytes 0.77. Urea 4.5, urate 0.24, glucose 11.5. ALT 138, albumin 33, bilirubin 23, sodium 142, potassium 3.9, creatinine 102 and alkaline phosphatase 206.

I have prescribed 2 weeks of treatment and will review him in a week's time.

Yours sincerely,

DR. A. ABOUTWERAT. MB, BCh, MSc, MRCP (UK)
Associate Specialist in Gastroenterology & Hepatology

cc: Dr. C. Hay,
Consultant Haematologist,
M.R.I.

DEPARTMENT OF GASTROENTEROLOGY
MANCHESTER ROYAL INFIRMARY
OXFORD ROAD
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C** Fax: **GRO-C**

Our ref AA/LR/M63/01420
NHS No 4523073333

Typed 12 August 02

Dr M W Mason
The Kiltearn Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Mason

Re: **Mr Paul BULLEN - DOB **GRO-C**1958**

GRO-C

I have reviewed Mr Bullen today he was off treatment for 2 weeks as his white blood cells and platelets were reduced due to Interferon treatment. Today his white bloods cells are 3.4, haemoglobin 12.2, platelets 55. I have re-commenced him on Viraferon peg 50 mcg once daily and Ribavirin 600 mg in divided doses. He will be reviewed again in 2 weeks time.

Yours sincerely

Dr A Aboutwerat MBBCh, MSc, MRCP (uk)
Associated Specialist in Gastroenterology and hepatology

DEPARTMENT OF GASTROENTEROLOGY
MANCHESTER ROYAL INFIRMARY
OXFORD ROAD
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: GRO-C Fax: GRO-C

Our ref AA/LR/M63/01420
NHS No 4523073333

Typed 17 September 02

Dr M W Mason
The Kiltarn Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Mason

Re: **Mr Paul BULLEN - DOB** GRO-C **1958**

GRO-C

Diagnosis Chronic hepatitis C, genotype 3
 Moderate haemophilia

Medication Viraferon peg 50 µgms per week and Ribavirin 600 mg per day.

I have reviewed Mr Bullen he continues to have symptoms of tiredness, but while on treatment he feels much better. His white blood cells are reduced at 1.8, neutrophils 1.01 and platelets 33. I think whilst his neutrophils are above 500 we will continue the same dose. I will discuss with Dr Hay as to whether any drug factors necessary to maintain his neutrophils and provide him with a larger dose of Viraferon to improve his chances of clearing viraemia. He will be reviewed in a couple of weeks time.

Yours sincerely

Dr A Aboutwerat MBBCh, MSc, MRCP (uk)
Associated Specialist in Gastroenterology and hepatology

Cc: Dr. C. Hay
 Consultant Haematologist
 MRI

Central Manchester and Manchester Children's University Hospitals



NHS Trust

DEPARTMENT OF GASTROENTEROLOGY
MANCHESTER ROYAL INFIRMARY
OXFORD ROAD
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: Fax:

Our ref AA/LR/M63/01420
NHS No 4523073333

Typed 17 September 02

Dr C Hay
Consultant Haematologist
M.R.I.

Dear Dr Hay

Re: Mr Paul BULLEN - DOB 1958

I would be grateful for your opinion regarding administration of growth factors (granulocyte stimulating factor) to allow us to continue with the treatment of Mr Bullen and give him the maximum chance of response. I see that some authorities are using this liberally to maintain high doses of Interferon. I welcome your opinion.

Yours sincerely

Dr A Aboutwerat MB Ch, MSc, MRCP (uk)
Associated Specialist in Gastroenterology and hepatology



Awarded for excellence

Incorporating:-
Royal Manchester Children's Hospital ♦ Manchester Royal Infirmary ♦ Manchester Royal Eye Hospital
Booth Hall Children's Hospital ♦ Saint Mary's Hospital for Women and Children ♦ University Dental Hospital of Manchester



Dr CRM Hay - Haemophilia Centre Director
Consultant Haematologist

Miss K Jones
Secretary to Dr CRM Hay

Telephone: +44 (0) **GRO-C**
Facsimile: +44 (0) **GRO-C**
E-mail: **GRO-C**
Our ref: CRMH/KT/M63/01420
NHS No.: 452 307 3333

Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology
Cobbe House (Orange Zone)
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

1 October 2002

Dr Aboutwerat
Associate Specialist in Gastroenterology and Hepatology
Department of Gastroenterology
MRI

Dear Dr Aboutwerat

Mr Paul Bullen DoB: **GRO-C1958**

GRO-C

Thank you for your enquiry. Interestingly I was considering giving GCFS in one of my other patients, with a dose limiting neutropenia on Peg Interferon and Ribavirin. There seems little doubt if one compromises with the dose, because of neutropenia there is a loss of anti viral efficacy. I think we could probably titrate the dose, since it is likely we would get away with a smaller dose than that required following chemotherapy. I would suggest that Mr Bullen comes to either a Wednesday afternoon or Thursday morning clinic and sees both of us. The cost of the GCFS will of course be considerable.

We tend to accept any neutrophil count above $.5 \times 10^9/l$ and give the maximum tolerable dose of Peg Interferon.

Yours sincerely

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Dr MW Mason
The Kiltearn Medical Centre
Hospital Street
Nantwich
Cheshire
CW5 5RL

Professor T W Warnes
Department of Gastroenterology
MRI

DEPARTMENT OF GASTROENTEROLOGY
MANCHESTER ROYAL INFIRMARY
OXFORD ROAD
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES Tel: **GRO-C** Fax: **GRO-C**

Our ref AA/LR/M63/01420
NHS No 4523073333

Typed 15 November 02

Dr M W Mason
The Kiltarn Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Mason

Re: **Mr Paul BULLEN - DOB: **GRO-C** 1958**
GRO-C

I have reviewed Mr Bullen today. He is currently on Week 20 anti viral treatment for chronic hepatitis C infection and his current medication is Viraferon peg 2µgms per week, Ribavirin 600 mgs per day. His full blood count remains abnormal but stable with neutrophils 1.2, platelets 39, white blood cells 2.1, haemoglobin 11.2. I have advised him to continue with the same dose and we will see him in 1 week's time.

Yours sincerely

Dr A Aboutwerat MBBCh, MSc, MRCP (UK)
Associated Specialist in Gastroenterology and hepatology

Cc: Dr C Hay
Consultant Haematologist
MRI

63/1420 Haem.

Central Manchester and Manchester Children's University Hospitals



Consultant Haematologist

Miss K Jones
Secretary to Dr CRM Hay

Telephone: +44 (0) **GRO-C**
Facsimile: +44 (0) **GRO-C**
E-mail: **GRO-C**

Dr CRM Hay - Haemophilia Centre Director
NHS Trust
Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology
Cobbett House (Orange Zone)
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

Our ref: CRMH/KT/

Professor T W Warnes
Consultant Physician
Department of Gastroenterology
Manchester Royal Infirmary

Dear Tom

Re: **Treatment of Hepatitis C**

15/11/12
T.W.
Warnes
7
series

Your registrar wrote to me recently specifically about Paul Bullen, whose neutropenia was leading to dose reductions. I did write back to him and to yourself about the use of GCSF to support the neutrophil count and permit fuller doses. Some people are also using Erythropoietin to avoid reduction in Ribavirin dose. We are finding only small doses of GCSF are required, as little as half a vial once a week, and are currently adopting an aggressive policy in which we attempt to maintain all patients on full dose treatment, even if this requires growth factor support.

It has become very clear to us and is also clear from the literature that dose reductions of both Interferon and Ribavirin lead to a loss of efficacy and are therefore to be avoided. We tend to titrate the dose so that we can manage the patients with the smallest dose possible, not least because GCFS also has flu like side effects and may lead to a worsening in the side effects of treatment of hepatitis C. If you wish us to become involved in Paul Bullen's management, so that we can optimise his treatment we would be very happy to do so. Perhaps we should even sit down and have a chat about our experience in this area.

With Best Wishes

Yours sincerely

GRO-C

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine



Incorporating:-
Royal Manchester Children's Hospital ♦ Manchester Royal Infirmary ♦ Manchester Royal Eye Hospital
Booth Hall Children's Hospital ♦ Saint Mary's Hospital for Women and Children ♦ University Dental Hospital of Manchester



Department of Clinical Haematology
Manchester Royal Infirmary
Cobbett House
Oxford Road
Manchester
M13 9WL

Tele: GRO-C Fax: GRO-C E-mail kjones@ GRO-C

Our ref kj/M63/01420
NHS No 4523073333

Clinic Date: 20 November 02

Typed 22 November 02

Dr Ali
Department of Gastroenterology
MRI

Dear Dr Ali

Re: **Mr Paul BULLEN - DOB** GRO-C **1958**
 GRO-C

Thank you for seeing this patient with me. He has severe haemophilia, cirrhosis of the liver secondary to chronic hepatitis C genotype 3. He has now completed about six months of Peg interferon and Ribavirin treatment. I note that he has been on most of this time on half doses of both drugs because of cytopenia. I am not quite sure why the Ribavirin was reduced to 600 mg a day since the lowest haemoglobin I could find was about 11.5 g. he has also been neutropenic and his neutrophil count has fallen as low as $0.83 \times 10^9/l$. most worrying is his platelet count. He does have portal hypertension and is permanently thrombocytopenic and his platelet count has fallen as low as 33, though it usually runs around the low 40's.

Paul's liver function tests have improved on treatment, but his ALT is still about 80.

I think it is extremely unlikely that he will obtain a complete remission on this reduced dose of treatment. On the other hand, I doubt that he will be able to tolerate full treatment because of his thrombocytopenia. I think it is worthwhile in the short term titrating his dose upwards to see what the maximum dose is that he could tolerate, using Lenograstim recombinant human GCSF to boost his white cell count and, if necessary, Erythropoietin to improve his haemoglobin. We have titrated the GCSF dose to achieve an acceptable white cell count and have found that patients tend to be extremely sensitive to quite small doses. Similarly I do not think much problem would be encountered supporting the haemoglobin and he ought to be able to tolerate full dose Ribavirin. My concern is that as we increase the Interferon the platelet count may fall to a dangerous level. I would be willing to contemplate a platelet count perhaps down as low as 25.

If he is unable to tolerate significantly higher doses of treatment than he currently has then I think there is an argument for discontinuing treatment altogether.

Yours sincerely

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Dr CRM Hay Consultant Haematologist, Honorary Senior Lecturer in Medicine

Dr M W Mason
The Kildarn Medical Centre
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dr CRM Hay Consultant Haematologist, Honorary Senior Lecturer in Medicine

DEPARTMENT OF GASTROENTEROLOGY

Manchester Royal Infirmary

Oxford Road

MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C**

Fax: **GRO-C**

email: twwarnes@ **GRO-C**

Our ref AA/JMH/M63/01420

NHS No 4523073333

Dr M W Mason
The Kiltearn Med Centre
Hospital Street
Nantwich
CW5 5RL

11 December 2002

Dear Dr Mason

Re: Mr Paul BULLEN - DOB **GRO-C 1958**

GRO-C

I saw this man on 4.12.02. He continues on Viraferon peg 60 µgm a week and Ribavirin 600 mg a day in two divided doses. His platelets are stable at 34, neutrophils just above 1. He also continues on Lenograstim recombinant human GCSF on a weekly basis.

I think we should continue on the same medication and review him in a week's time. It may be possible that we increase the Ribavirin to 400 mg b.d.

Yours sincerely,

DR. A. ABOUTWERAT. MB, BCh, MSc, MRCP (UK)
Associate Specialist in Gastroenterology & Hepatology

Department of Gastroenterology
Manchester Royal Infirmary
Oxford Road
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C** Fax: **GRO-C**

Our ref AA/LR/M63/01420
NHS No 4523073333

Clinic Date: 02 January 03

Typed 08 January 03

Dr M W Mason
The Kildare Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Mason

Re: **Mr Paul BULLEN - DOB **GRO-C** 1958**
GRO-C

Diagnosis Chronic hepatitis C with cirrhosis genotype 3
Severe haemophilia

Medication Viraferon peg 65µgm per week, Ribavirin 400 mg bd., Lenograstim recombinant human GCSF 105µgm
per week

I have reviewed Paul today. He is keeping well and asymptomatic. I have arranged his liver function, full blood count, prescribed the treatment and will reassess his condition in a week's time.

Yours sincerely

DR. A. ABOUTWERAT MBBCh, MSc, MRCP (UK)
Associated Specialist in Gastroenterology and hepatology

Cc: Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology

Manchester Haemophilia Comprehensive Care Centre

Department of Clinical Haematology
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL

PA/Medical Secretary to Dr CRM Hay: Ms Kim Jones Direct phone/fax No.: GRO-C E-mail: GRO-C

Our ref: kj/M63/01420
NHS No: 4523073333

Typed: 28 January 03
Clinic Date: 22 January 03

Dr A Aboutwerat
Associate Specialist in Gastroenterology
Dept of Gastroenterology
Manchester Royal Infirmary

Dear Dr Aboutwerat

Re: Mr Paul BULLEN - DOB GRO-C 1958

GRO-C

Diagnosis: Moderate Severity Haemophilia
Hepatitis C
Cirrhosis of the Liver

I saw Paul for review today. I see that he is maintaining a steady platelet count of about $35 \times 10^9/l$, which is just about acceptable. His neutrophil count is being propped-up with GCSF, which I note you have just increased to twice weekly. I think he probably manages once weekly to be honest, but he seems to be tolerating the GCSF better than average. Sadly, this will do nothing for his low platelet count and I note that he is still only on 65µg of pegylated Interferon plus Ribavirin. Since increasing his pegylated Interferon slightly his LFTs have improved further, but remain abnormal. I note that he has had a hepatitis C RNA test today, which I would expect to be positive. I doubt that we will be able to clear his virus on this dose and, at the same time, I doubt that he will be able to tolerate anything approaching full-dose, which is 120µg once a week. We could try edging the dose up a little bit further, but I do not think you will be able to increase his dose very much before he develops clinically significant thrombocytopenia complicated by bleeding.

We will review Paul again in 6-8 weeks' time.

Yours sincerely

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Dr M W Mason
The Kiltearn Medical Centre
Hospital Street
Nantwich
Cheshire CW5 5RL

Dr CRM Hay - Consultant Haematologist, Honorary Senior Lecturer in Medicine

Central Manchester and Manchester Children's University Hospitals



NHS Trust
Department of Gastroenterology
Manchester Royal Infirmary
Oxford Road
MANCHESTER M13 9WL

PROFESSOR T.W. WARNES

Tel: **GRO-C** Fax: **GRO-C**

Our ref: AA/LR/M63/01420
NHS No: 4523073333

Clinic Date: 02 April 03

Typed: 07 April 03

Dr J H Knapman
The Kilearn Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Knapman

Re: **Mr Paul BULLEN - DOB** **GRO-C** **1958**
GRO-C

Diagnosis Chronic hepatitis C infection
Most recent hepatitis C RNA by PCR was negative
Liver cirrhosis
Moderately severe haemophilia

I have reviewed Paul today. I am pleased to say that his most recent hepatitis C RNA by PCR was negative indicating absence of viraemia and it is very reassuring as he would like to be off treatment during the wedding of his daughter. I will ask him to discontinue the treatment on the 1st May 2003. By that time he will have had about 11 months of treatment although the dose was small but his liver function has much improved after the antiviral treatment and if he relapses we will probably offer him a further course of antiviral treatment. I will review him in June.

Yours sincerely

GRO-C

DR. A. ABOUTWATER MBBCh, MSc, MRCP (UK)
Associated Specialist in Gastroenterology and hepatology

Cc: Dr CRM Hay
Director Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology



Incorporating:-
Royal Manchester Children's Hospital ♦ Manchester Royal Infirmary ♦ Manchester Royal Eye Hospital
Booth Hall Children's Hospital ♦ Saint Mary's Hospital for Women and Children ♦ University Dental Hospital of Manchester



Manchester Haemophilia Comprehensive Care Centre

Department of Clinical Haematology
Manchester Royal Infirmary
Oxford Road
Manchester
M13 9WL
UK

PA/Medical Secretary to Dr CRM Hay: Ms Kim Jones

Direct phone/fax no. +44 (0) 161 275 4444

GRO-C

E-mail: gro-c@man.ac.uk

Our ref: kj/M63/01420

NHS No: 4523073333

Typed: 22 April 03

Dr A Aboutwerat
Associate Specialist in Gastroenterology & Hepatology
Department of Gastroenterology
Manchester Royal Infirmary

Dear Dr Aboutwerat

Re: **Mr Paul BULLEN - DOB: 1958**

GRO-C

I am pleased to hear that Paul is PCR negative. I realise that the patient is putting everyone under a lot of pressure to stop his treatment to cover the wedding of his daughter. On the other hand, he has only just become PCR negative after a prolonged period of treatment, which one would normally consider sub-optimal, which was limited by dose-related side effects. My own inclination would not be to compromise. I think his risk of relapse is extremely high and frankly I would push the dose as hard as I could for a bit longer.

Yours sincerely

Dr CRM Hay
Director, Manchester Haemophilia Comprehensive Care Centre
Honorary Senior Lecturer in Medicine

Dr J H Knapman
The Kiltearn Medical Centre
Hospital Street
Nantwich
Cheshire CW5 5RL

Dr CRM Hay - Consultant Haematologist, Honorary Senior Lecturer in Medicine

Department of Gastroenterology
Manchester Royal Infirmary
Oxford Road
MANCHESTER M13 9WL

Professor TW Warnes

Tel: **GRO-C**

Fax: **GRO-C**

Our ref: CF/LR/M63/01420
NHS No: 4523073333

Clinic Date: 04 June 03

Typed: 06 June 03

Dr J H Knapman
The Kiltarn Med Ctr
Hospital Street
Nantwich
Cheshire
CW5 5RL

Dear Dr Knapman

Re: Mr Paul BULLEN - DOB: **GRO-C 1958**
GRO-C

I saw Mr Bullen in clinic today. He is now approximately 1 month post combination therapy for his hepatitis C. During his treatment he was demonstrated to become HCV PCR negative and I have checked this again today. He also had his LFT's and FPC repeated and will see him in clinic in 6 months time. We hope that he remains clear of the virus.

Yours sincerely

Dr C Fraser
Specialist Registrar in Gastroenterology

Cc: Dr CRM Hay
Director Manchester Haemophilia Comprehensive Care Centre
Department of Clinical Haematology