高雄醫學大學附設中和紀念醫院
Kaohsiung Medical University Chung-Ho Memorial Hospital
人體試驗審查委員會
Institutional Review Board

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人體研究新案同意證明書

計畫中文名稱：一個交叉試驗，評估提高鐵劑劑量與原本鐵劑使用量在治療血液透析的療效及安全性
計畫主持人：林祐賢
共同及協同主持人：鈕聖文、郭宜瑾
研究人員：無
機構名稱：高雄市立大同醫院
經費來源：院內計畫
IRB 編號：KMUHIRB-F(I)-20190110
計畫編號：NA
核准日期(審查通過日)：2019/9/20
計畫執行期間：2019/9/20-2022/12/31
本同意書有效期限：2020/9/19
計畫書：2019 年 7 月 29 日
受試者同意書：2019 年 7 月 29 日
中文摘要：2019 年 7 月 29 日
英文摘要：2019 年 7 月 29 日

未預期事件或藥品嚴重不良反應通報、後續定期追蹤之程序及應注意事項，請參閱背面。

高雄醫學大學附設中和紀念醫院
第一人體試驗審查委員會
主任委員：顏學偉

西元 2019 年 9 月 20 日

Approval of Clinical Trial/Research

Protocol Title: *A cross-over trial to evaluate the efficacy and safety between increasing the dose of iron and original iron dosage in patients with mainta hemodialysis*
Principal Investigator: *You-Hsien Lin*
Co_Investigator(s): *Sheng-Wen Niu, I-Ching Kuo*
Study Coordinator: *NA*
Institution: *Kaohsiung Municipal Ta-Tung Hospital*
Source of Funding: *Institutional Program*
IRB Number: *KMUHIRB-F(I)-20190110*
Protocol Number: *NA*
Approval Date: *2019/9/20*
Duration of Approval: *2019/9/20-2022/12/31*
Expiration Date of Approval: *2020/9/19*
Protocol: 2019/7/29
Informed Consent Form: 2019/7/29
Chinese Protocol Synopsis: 2019/7/29
English Protocol Synopsis: 2019/7/29

See the back of this page for the procedures for reporting unanticipated problems, or drug serious adverse reactions, or interim, and other important notes.

Hsueh-Wei Yen

Hsueh-Wei Yen, MD, PhD
Chairman
Institutional Review Board-I
Kaohsiung Medical University
Chung-Ho Memorial Hospital

	人體(■試驗/□研究) 受試者同意書	文件編碼	KMUH/IRB/AF/08E-03/000
		SOP 版次	第 11 版

我們邀請您參加本人體試驗，此份同意書提供您本研究相關資訊，計畫主持人或研究人員將為您詳細說明並回答相關問題。

計畫名稱

中文：**一個交叉試驗，評估提高鐵劑劑量與原本鐵劑使用量在治療血液透析的療效及安全性**

英文：A cross-over trial to evaluate the efficacy and safety between increasing the dose of iron and original iron dosage in patients with maintenance hemodialysis

IRB 編號	KMUHIRB--F(I)-20190110	**計畫編號**	NA
研究執行期限	自 IRB 通過日起至 2022 年 12 月 31 日		
試驗機構： 大同醫院腎臟內科	委託單位/藥廠： 無		

■藥品 □醫療器材 □新醫療技術 □人體研究 □其它：_____

收案地點：□高醫大 □高醫附院 □小港醫院 ■大同醫院 □旗津醫院
□其他：_____

計畫主持人： 林祐賢醫師 單位：大同內科 電話：07-3223627 ext 8736
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二十四小時緊急聯絡人：林祐賢醫師 手機號碼：0975356145

1. 藥品/醫療器材全球上市現況簡介：□不適用
喜鐵福注射液已經於全球上市

2. 研究背景/試驗目的：
靜脈注射鐵是接受血液透析的患者的標準治療方法，2019年1月美國新英格蘭雜誌NEJM 2019 Jan 31;380(5):447-458刊載(Proactive IV Iron Therapy in Haemodialysis Patients, PIVOTAL, 血液透析患者的主動靜脈鐵治療) 臨床試驗, 研究結果發現，比傳統劑量高的鐵劑治療可以改善透析病人心血管預後、輸血次數、與紅血球生成素使用量。大同醫院血液透析室依照(Kidney Disease Improving Global Outcomes, KDIGO, 腎病改善全球預後)準則，目前鐵劑治療準則為當Ferritin (鐵蛋白)>500ng/ml, 或(transferin saturation, TSAT, 運鐵蛋白飽和度)>20%停止給予病患鐵劑治療。因此我們將依照NEJM建議修改鐵劑治療準則，提高大同醫院透析室鐵劑治療劑量。

本試驗是一個第四期，(台灣單中心)的臨床試驗，預計全球收納200人，台灣收納200人。本試驗目的為評估治療末期腎病變貧血症的效果，當提高鐵劑給予量的治療效果與安全性。任何治療都有風險存在，臨床試驗也不例外，請您在詳細思考後再決定是否參加本試驗。

高醫 人體試驗委員會 2019-09-20 審查通過

3. 試驗之主要納入與排除條件：

3.1 納入條件(符合下列條件者，適合參加本研究)

- 您必須年滿20歲
- 您必須在過去3個月內未曾捐血超過500cc
- 您必須能在試驗的24個月當中定其於本院透析室接受透析。

3.2 排除條件(若有下列情況者，不能參加本研究)

- 您有惡性腫瘤接受化學治療
- 你過去未接受過鐵劑治療
- 您曾經對鐵劑過敏
- 您肝指數異常
- 您處於感染狀態

4. 試驗方法及相關檢驗：

若您決定加入本研究且簽署這份同意書後，我們將會對您進行體檢，體檢項目包括血液及尿液檢查，身高體重，心跳血壓測量。如果您的條件符合，您將開始於透析療程中依照血色素數值給予鐵劑，並按照試驗流程，定期追蹤血色素，若血色素達標，將會減量，或暫停鐵劑給予。

為確保研究結果不被人為扭曲，本試驗為非隨機前後對照研究。將會比較進入試驗前您的臨床狀況與進入後您的臨床狀況進行分析比較。

試驗藥物

喜鐵福注射液(蔗糖鐵)，每小瓶水溶液注射劑，含100mg的鐵（5mL）。

試驗程序

篩選期（第-7至-1天）

試驗藥物在第1個療程前的一週內，試驗人員將會向您說明試驗內容，並請您簽署受試者同意書。

若您同意參加本試驗，試驗人員將需要取得下列資訊及評估結果：

身高、體重、年齡、性別、血色素、白血球、血小板、血清鐵質、儲鐵蛋白、運鐵蛋白飽和度。

治療期（第1療程）-第8（±3）天與第15（-3至+7）天

本次回診期間，您需要接受下列程序：

血色素檢測

2.檢體及剩餘檢體之部分類型(檢體類型可依計畫書內容自行增減)

一般生化、血液檢驗檢體

生物標記檢體/遺傳學檢體

在試驗期間，會將您的檢體送往林祐賢醫師的大同醫院地下一樓共同實驗室進行處置、處理與進一步分析。此機構地址為高雄市中華三路68號。中央實驗室不會在分析後將實驗室結果提供給試驗中心。完成試驗後，若有剩餘檢體，將保存於大同醫院地下一樓，最長將保存10年。

個人資料

在試驗期間，依據試驗計畫類型與您所授權的內容，我們將會蒐集與您有關的病歷資料、醫療記錄、量表、問卷等資料與資訊，並以一個試驗編號來代替您的名字及相關個人資料。前述資料與資訊若為紙本型式，將會與本同意書分開存放於試驗機構之上鎖櫃中；若為電子方式儲存或建檔以供統計與分析之用，將會存放於設有密碼與適當防毒軟體之專屬電腦內（本段有關紙本與電子資料之保存管理事宜，僅為撰寫範例，得依各試驗案實際狀況酌予補充與修正）。所有資料與資訊將會保存至藥品於我國上市後至少兩年，若試驗藥品終止研發則保存至試驗正式停止後至少二年，至多將保存至藥品上市後或試驗正式停止後10年，屆時將予以銷毀。上述資料與資訊若傳輸至國外分析與統計，您仍會獲得與本國法規相符的保障，計畫主持人與相關團隊將盡力確保您的個人資料獲得妥善保護。

6. 可能產生之副作用、發生率及處理方法：

3. 與試驗藥物相關的風險 (本試驗使用藥物的副作用)

所有試驗藥物都可能造成副作用，而您可能會經歷也可能不會發生下列的副作用。

副作用：

A副作用(發生率<1%)

藥物外漏, 處理方式: 鐵劑滲漏至輸液處局部組織，滲漏後可引起疼痛、炎症反應、局部褐色變，嚴重時發生壞死。通常不需特殊處理，嚴重時則需要外科處置。

B副作用(發生率<1%)

輸注鐵劑時有時會出現低血壓，可能與輸注過快、預防性使用抗組胺藥有關，通常無需特殊處理，如果不恰當的給予升血壓藥反倒可能會引起血液動力學異常。

C副作用(發生率<1%)

靜脈鐵劑產生的羥基自由基也能損傷肝臟，為避免出現鐵過載，鐵過載是持續加重肝臟損傷的因素。本研究排除肝功能異常者

D副作用(發生率<1%)

靜脈補鐵時血流中有較多的游離鐵，有助於細菌生長。因此本研究排除有感染者。

E副作用(發生率<1%)

對有多種藥物過敏史、特應性過敏史、全身炎症性疾病如系統性紅斑狼瘡和類風濕關節炎的患者，使用靜脈鐵劑時我們會格外謹慎，因其發生過敏反應的機會更大。鐵劑試敏即

使陰性並不意味著不發生高敏反應，縱使現在一些鐵劑無需試敏，我們每次使用鐵劑時也會至少要嚴密監測 30 分鐘。輕者無需處理，重者如處理不及時可能會危脅生命。常見反應包括：

（1）輕度包括皮膚癢感、潮紅、發熱、胸部緊束感、蕁麻疹、背痛、高血壓。

（2）中度除了包括輕度症狀外，還可以有咳嗽、噁心、呼吸困難、心動過速和低血壓。

（3）重度時症狀重、多且出現突然，包括哮鳴、眶周水腫、發紺、喪失意識、心臟或呼吸驟停。

F副作用(發生率<1%)

提高鐵劑劑量會造成因為鐵過載造成其他器官損傷，最常過載於肝臟器官，我們會密切監測 TSAT, 我們也會密切追蹤肝指數(GOT, GPT), 疑似過再將立刻停止鐵劑給予，並安排核磁共振，若有必要更進一步安排肝切片確診。

發生副作用時: 立即停止注射，密切監控生命徵象，若有必要給予抗過敏藥物。

本試驗可能會有其他的副作用，但目前還不清楚。參加試驗期間，試驗醫師及其他試驗人員會定期監測您是否發生副作用。必要時，將安排您進行額外的訪視及檢測。如果您發生副作用，敬請告知您的試驗醫師及其他試驗人員，試驗醫師會依您的情況決定給予適當處置。

4.與試驗過程相關的風險

在試驗進行的過程中，您可能會感到不適，某些檢驗可能會有危險，例如：採集血液樣本、心電圖檢測、肝臟切片檢查...等。

- 採集血液樣本：從手臂上抽血可能會引起部位疼痛、瘀青、頭昏眼花，而在很低的機率下可能會發生感染。處理方式為抽血後需按壓抽血部位至少 5 分鐘；瘀青可以熱敷方式緩解；頭昏眼花則需靜坐或平躺休息。若抽血處感染請立即與本研究主持人林祐賢醫師聯絡，大同醫院將提供您必要之醫療照護

如果您出現任何上述嚴重或危險的副作用，您應該儘速：

1. 撥打電話聯絡24小時緊急聯絡人。

視需要前往最近的急診室。

心理方面—受試者因參與本試驗時可能會產生之心理影響，如對於透析因貧血需要額外接受治療感到壓力。

社會方面—受試者及其親屬或族群可能造成的影響，如對於加入臨床試驗感到壓力。

7. 其他替代療法及說明：

您不一定要參與本試驗才能改善您的疾病。若不參與本試驗，您的疾病也可接受原本鐵騎劑量治療，包括已核准或已使用於治療您此種疾病的藥物。您的試驗醫師可與您討論這些替代療法的風險與優點。此外，您也可以跟您的例行照護醫師討論您的選擇。

8. 試驗預期效益：

在過去的人體使用經驗中顯示當鐵劑劑量升高可以改善貧血，減少輸血機率。

即便有以上資料，仍不能保證參加本試驗您的病情一定會因此好轉或為您本人帶來其他直接的好處。

參加本試驗有哪些可能的益處？

您可能不會因為參加本試驗而獲得利益。試驗是供醫師了解藥物能否有效對抗疾病的方式。您參加本試驗所獲得的資訊，可能會幫助治療血液透析的患者更加了解療效及安全性。在未來也可能嘉惠其他患有相同疾病的病患。

9. 試驗進行中受試者之禁忌、限制與應配合之事項：

當您參加本試驗期間，為了您的安全，請您配合以下事項：

-不應再參加其他臨床研究。

-提供您的過去病史、醫療紀錄及和目前病情有關的正確資訊

-為了您的安全，請按照約定時間返診，若原約定時間無法前來，也請您和試驗人員聯絡。-請按時填寫日誌如實記錄您的病情。(依計畫書)

-為了您的安全，請告知試驗醫師您出現的任何不舒服症狀。

-不可任意服用其他藥物，包括成藥、中草藥、健康食品等，若有需要使用其他藥物，請和您的試驗醫師討論。(依計畫書)

-若其他醫師有開新藥或改變使用藥物，即使是和試驗無關的疾病，請告知試驗醫師。

-若您有任何疑問，請不要客氣，請和您的試驗人員(醫師、護士)直接提出。

-請勿懷孕或讓人懷孕。若您仍有可能懷孕或讓人懷孕，試驗期間請使用高效率避孕法，例如：子宮內避孕器、賀爾蒙避孕藥。(依計畫書)

-若您在其他醫療院所臨時就醫，請和醫療人員表明您有在使用某種試驗藥物。

-如果您在兩次回診之間曾住院或醫療狀況出現變化，或是您希望停止使用試驗藥物(或已經停藥)，請通知您的試驗醫師。

10. 研究結束後資料/檢體處理方法：

□同意以非去連結之方式繼續提供高雄醫學大學及高雄醫學大學附屬機構、相關事業從事其他方面研究，若超出我同意使用檢體的範圍，經原主治醫師轉介，再次得到我的同意，才可使用我的檢體進行新的研究，且該份同意書和研究計畫必須先通過高雄醫學大學附設中和紀念醫院人體試驗審查委員會的審查。

□同意捐贈高雄醫學大學及高雄醫學大學附屬機構、相關事業人體生物資料庫保存（經去連結後，可做後續醫學研究，絕不涉及個人隱私）。

□由高雄醫學大學及高雄醫學大學附屬機構、相關事業銷毀。

□歸還（鑒於剩餘檢體可能為病灶組織，其保存及攜帶亦可能具有感染之危險性，建議如無特殊需求及保存設備，由高雄醫學大學及高雄醫學大學附屬機構、相關事業代為銷毀）。

11. 試驗之醫學倫理考量：

研究人員於進行研究前先經由人體試驗審查委員會審查通過，並遵循醫學倫理的自主、不傷害、及公平等三大原則。在自主原則方面，研究人員於進行收案前，會評估您的身心狀況，符合條件後再向您仔細說明研究主題、目的及進行方式，確保您接受充足之資訊、並經理性思考、於未受脅迫或操控之情形下，自願參與試驗，徵得您的同意且填妥同意書後才開始進行。在研究進行期間，您有絕對的自主權，可隨時決定退出本研究，且絕對不影響就醫或治療權利及照護品質。在不傷害原則方面，本研究以尊重人權及倫理的考量為優先，任何可辨識您的身分資料都會利用編碼方式處理加以保密，所有研究中所收集到的資料，僅供學

術研究之參考，僅在您允許知情況中公開。參與研究同意書及研究結果將會分開置放並妥善保存以確保您所提供之資料不外洩。在公平原則方面，收案對象不因其社經地位、個人特質、種族、性別或健康狀況而有不同的待遇。研究進行中，會即時提供給與您的健康或是疾病相關資訊，並將會提供您任何與研究相關問題之諮詢方式及聯絡電話，以達公平性。

12. 機密性：

林祐賢醫師 將依法將您的資料作為機密處理，於研究期間，檢體/資料將以代碼取代受試者個人資料，以保障受試者隱私。您亦了解臨床試驗監測者、稽核者、主管機關與本院人體試驗審查委員會皆有權檢視您的研究資料，以確保臨床試驗過程或數據符合相關法律及法規要求，並會遵守保密之倫理。

13. 研究成果用途

1. 本計畫研究成果將發表於學術期刊。
2. 如本計畫研究成果獲得學術文獻發表時，您同意無償贈與高雄醫學大學/高雄醫學大學附設中和紀念醫院/高雄市立小港醫院/高雄市立大同醫院作為從事疾病診斷、預防、治療及研究等醫學用途。

14. 補助、所需費用、損害賠償與保險

A. 參加試驗之補助：
   i 本試驗無任何補助。

B. 經費負擔：
   i 參加本試驗您不需負擔任何與本試驗相關之費用。如依本研究所訂臨床試驗計畫，因發生不良反應造成損害，由試驗執行機構__ ■大同醫院依法負賠償及補償責任。但本受試者同意書上所記載之可預期不良反應，不予補償。

C. 如依本研究所訂臨床試驗計畫，因而發生不良反應或損害，本醫院願意提供專業醫療照顧及醫療諮詢。

D. 除前二項補償及醫療照護外，本研究不提供其他形式之補償，若您不願意接受這樣的風險，請勿參加試驗。

E. 您不會因簽署本同意書，而喪失在法律上的任何權益。

F. 本研究未投保責任保險。

15. 受試者權利：

A. 試驗過程中，與你(妳)的健康或是疾病有關，可能影響你(妳)繼續接受臨床試驗意願的任何重大發現，都將即時主動提供給你(妳)。

B. 為進行研究工作，你(妳)必須接受林祐賢醫師/鈕聖文醫師/郭宜瑾醫師的照顧。如果你(妳)現在或於試驗期間有任何問題或狀況，請不必客氣，可與計畫主持人林祐賢醫師聯絡（24 小時聯繫電話：0975356145）。

本同意書一式二份，研究人員已將同意書副本交給你(妳)，並已完整說明本研究之性質與目的。研究人員林祐賢醫師已回答您有關藥品/研究的問題。

C. 如果你(妳)在試驗過程中對試驗工作性質產生疑問，對身為患者之權利有意見或懷疑因參與研究而受害時，可與本院之人體試驗審查委員會聯絡請求諮詢，其電話號碼為：07-3121101 分機 6646 或 07-3133525。

D. 本研究計畫書已經由人體試驗審查委員會(Institutional Review Boards, IRB)審查通過才能執行。人體試驗審查委員會是依衛生福利部規定由具醫學背景之專業人員與非醫學背景之社會公正人士所共同組成，為獨立運作之委員會，執行審查、核准及監督人體研究案，以保護研究對象之權利、安全與福祉。

E. 人體試驗審查委員會審查研究計畫，綜合評估研究方法及程序之適當性，尊重研究對象之自主權，確保研究進行之風險與利益相平衡，對研究對象侵害最小，並兼顧研究負擔與成果之公平分配，以保障研究對象之權益。

F. 任何研究案皆有風險，請您謹慎評估！

16. 試驗之退出與中止：

您可自由決定是否參加本試驗；試驗過程中也可隨時撤銷同意，退出試驗，不需任何理由，且不會引起任何不愉快或影響其日後醫師對您的醫療照顧。林祐賢醫師【試驗主持人或試驗委託者】亦可能於必要時中止該試驗之進行，當試驗中止或終止時，林祐賢醫師【試驗主持人或試驗委託者】將立即通知您並確保您有適當之治療及追蹤

17. 中途退出後資料/檢體處理方法：

□同意以非去連結之方式繼續提供高雄醫學大學及高雄醫學大學附屬機構、相關事業從事其他方面研究，若超出我同意使用檢體的範圍，需再次得到我的同意才可使用我的檢體進行新的研究，且該份同意書和研究計畫必須先通過高雄醫學大學附設中和紀念醫院人體試驗審查委員會的審查。

□同意捐贈高雄醫學大學及高雄醫學大學附屬機構、相關事業人體生物資料庫保存（經去連結後，可做後續醫學研究，絕不涉及個人隱私）。

□由高雄醫學大學及高雄醫學大學附屬機構、相關事業銷毀。

□歸還（鑒於剩餘檢體可能為病灶組織，其保存及攜帶亦可能具有感染之危險性，建議如無特殊需求及保存設備，由高雄醫學大學及高雄醫學大學附屬機構、相關事業代為銷毀）。

18.研究預期可能衍生之商業利益：

本研究預期不會衍生專利權或其他商業利益。

19. 簽名

1.試驗主持人、或協同主持人或其授權人員已詳細解釋有關本研究計畫中上述研究方法的性質與目的，及可能產生的危險與利益。

試驗主持人/協同主持人簽名：_____日期：_____年____月____日

在取得同意過程中其他參與解說及討論之研究人員簽名：_____日期：_____年____月____日

2.經由說明後本人已詳細瞭解上述研究方法及可能產生的危險與利益，有關本試驗計畫的疑問，亦獲得詳細解釋。本人同意接受並自願參與本研究，且將持有同意書副本。

受試者簽名：　　日期：＿＿＿＿年＿＿＿月＿＿＿日

出生年月日：＿＿＿＿年＿＿＿月＿＿＿日　電話：

國民身分證統一編號：　　性別：

通訊地址：

□受試者為無行為能力人（未滿七歲之未成年人）或受監護宣告之人時，應得其法定代理人或監護人之同意。

□受試者為限制行為能力人（七歲以上未滿二十歲之未成年人）或受輔助宣告之人時，應得其本人及法定代理人或輔助人之同意。

□受試者雖非無行為能力、限制行為能力或受監護宣告、受輔助宣告者，但因無意識或精神錯亂無法自行為之時，由有同意權之人為之。前項有同意權之人順序為(1)配偶(2)成年子女(3)父母(4)兄弟姐妹(5)祖父母。

※法定代理人/監護人/輔助人/有同意權人

簽名：　　日期：　　年　　月　　日

與受試者關係：　　聯絡電話：

通訊地址：

A. 茲證明計畫主持人已完整地向受試者解釋本研究的內容。

見證人簽名：　　日期：　　年　　月　　日

※1. 受試者、法定代理人/監護人/輔助人或有同意權之人皆無法閱讀時，應由見證人在場參與所有有關受試者同意書之討論。見證人應閱讀受試者同意書及提供受試者之任何其他書面資料，以見證試驗主持人或其指定之人員已經確切地將其內容向受試者、法定代理人或有同意權之人解釋，並確定其充分了解所有資料之內容。

2. 受試者、法定代理人/監護人/輔助人或有同意權之人，仍應於受試者同意書親筆簽名並載明日期。但得以指印代替簽名。

3. 見證人於完成口述說明，並確定受試者、法定代理人或有同意權之人之同意完全出於其自由意願後，應於受試者同意書簽名並載明日期。

4. 試驗相關人員不得為見證人。

	Human body (■Trial/□Research) Subject consent	File Coding	KMUH/IRB/AF/08E-03/000
		SOP Edition	The 11th edition

We invite you to participate in this human experimental trial. This consent form provides you with relevant information about this study. The project host or researcher will explain and answer relevant questions in detail for you.

Project name: A cross-over trial to evaluate the efficacy and safety between increasing the dose of iron and original iron dosage in patients with maintenance hemodialysis

IRB Number	**KMUHIRB**-F(I)-20190110	**Project Number**	
Research execution deadline	From the date of IRB adoption to December 31, 2022		
Trial institution: Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, KMUH	Entrusted unit/pharmaceutical factory: no		

■Drugs □Medical equipment □New medical technology □Human body research □Others: _____

Place of collection: □Kaohsiung Medical University □Kaohsiung Medical University Hospital □Xiaogang Hospital, KMUH ■Kaohsiung Municipal Ta-Tung Hospital, KMUH □Qijin Hospital, KMUH
□Others:
Project host: Dr. Hugo Y.-H. Lin Unit: Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, KMUH Telephone: +886-7-2911101 ext 8736
Co-host: Dr. Sheng-Wen Niu Unit: Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, KMUH Tel: +886-7-2911101 ext 8736
Co-host: Dr. I-Ching Kuo Unit: Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, KMUH Tel: +886-7-2911101 ext 8736
24-hour emergency contact: Dr. Hugo Y.-H. Lin, Mobile phone number: +886-975356145

1. Brief introduction of the global market status of pharmaceuticals/medical devices: □Not applicable
Sucrofer injection has been listed globally

2. Research background/test purpose:
Intravenous iron is the standard treatment for patients undergoing hemodialysis. In January, 2019,

the New England Journal NEJM 2019 Jan 31; 380(5): 447-458 (Proactive IV Iron Therapy in Haemodialysis Patients, PIVOTAL, hemodialysis patients Active venous iron therapy) clinical trial, this study found that iron therapy higher than traditional doses can improve cardiovascular prognosis, blood transfusion times, and erythropoietin use in dialysis patients. The hemodialysis room of Ta-Tung Hospital follows the (Kidney Disease Improving Global Outcomes, KDIGO, Kidney Disease Improvement Global Prognosis) guidelines. The current iron treatment guidelines are iron therapy until Ferritin (ferritin)>500ng/ml, or (transferin saturation, TSAT, transferrin saturation Degree)>20%. Therefore, we revise the iron treatment guidelines according to the NEJM recommendation and increase the iron treatment dose in the dialysis room of Datong Hospital.
This trial is a Phase IV (Taiwan Single Center) clinical trial. It is expected to accommodate 200 people in Taiwan. The purpose of this trial is to evaluate the effect of treating end-stage renal disease anemia, and to increase the therapeutic effect and safety of iron dose.
There are risks in any treatment, and clinical trials are no exception. Please decide whether to participate in this trial after careful consideration.

3. The main inclusion and exclusion conditions of the experiment:

3.1 Inclusion conditions (people who meet the following conditions are suitable to participate in this study)

• You must be at least 20-year-old.

• You must not have donated more than 500cc of blood within the past 3 months.

• You must be able to get dialysis in the dialysis room of our hospital within 24 months of the trial.

3.2 Exclusion conditions (If you have the following conditions, you can not participate in this study)

• You have malignant tumor receiving chemotherapy.

• You have not received iron treatment in the past.

• You have been allergic to iron.

• Your liver function test is abnormal.

• You are in infection status.

4. Test method and related inspection:
If you decide to join this study and sign this consent form, we will conduct a physical examination for you. The physical examination items include blood and urine examination, height and weight, and heartbeat blood pressure measurement. If your conditions are met, you will start to give iron according to the hemoglobin value during the dialysis treatment, and follow up the hemoglobin regularly according to the test process. If the hemoglobin meets the standard, it will be reduced or the iron administration will be suspended.
You will compare your clinical status before entering the trial with your clinical status after entering.

Test drug

Sucrofer injection (iron sucrose), each vial of water injection contains 100mg of iron (5mL).

Test procedure
Screening period (days -7 to -1)
Test drug within one week before the first course of treatment, the test staff will explain the test content to you and ask you to sign the subject's consent form. If you agree to participate in this trial, the trial staff will need to obtain the following information and evaluation results:
Height, weight, age, sex, hemoglobin, white blood cells, platelets, serum iron, ferritin, transferrin saturation.
Treatment period: after enrollment until 2022.
During this return visit, you need to undergo the following procedures:
Hemoglobin detection.

5. How the data/sample will be processed, where and how long it will be stored, who can use your sample:

1. Preservation and use of specimens and remaining specimens

(1) Preservation and use of specimens (including their derivatives)

For the purpose of research, our specimens collected by us will be used in accordance with this research plan. The specimens will be stored in the common laboratory on the ground floor of Ta-Tung Hospital. Until the expiration date of 2032, we will destroy them according to law. In order to protect your personal privacy, we will replace your name and related personal data with a test number to confirm that your specimen and related data are completely confidential. If you have doubts about the use of the specimen, or you have any need to destroy the specimen, please contact us immediately (contact person: Dr. Hugo Y.-H. Lin, telephone: +886-7-2911101 ext. 8736), we will destruct immediately. You can also contact (Kaohsiung Medical University Hospital Intituional Review Board, KMUIRB) to assist you in resolving any disputes regarding the research use of the specimen.

(2) Reuse of remaining samples (including derivatives)

All new research plans must be reviewed and approved by the KMUIRB. If the KMUIRB determines that the new research is beyond the scope of your consent, it will require us to obtain your consent again.

Do you agree that the remaining samples will be reserved for future research by Dr. Lin, and authorize the KMUIRB to review whether you need to obtain your consent again (choose one)

□ I do not agree to save my remaining samples, please destroy them after the test is over.

□ I agree to save my remaining specimens in a non-disconnected manner. If the scope of the original consent is exceeded, my consent must be obtained again to use my specimens for new research.

2. Some types of specimens and remaining specimens

General biochemical and blood test specimens

Biomarker specimens/genetics specimens

During the trial period, your specimen will be sent to the joint laboratory on the ground floor of Kaohsiung Municipal Ta-Tung Hospital, KMUH of Dr. Hugo Y.-H. Lin for disposal, processing and further analysis. The address of this institution is No. 68, Zhonghua 3rd Road, Kaohsiung City. The central laboratory will not provide laboratory results to the test center after analysis. After the test is completed, if there are any remaining specimens, they will be stored on the ground floor of Kaohsiung Municipal Ta-Tung Hospital, KMUH for up to 10 years.

Personal information

During the trial period, we will collect chart records, medical records, scales, questionnaires and other data and information related to you based on the type of trial plan and the content authorized by you, and use a trial number to replace your name and related personal data. If the aforementioned data and information are in paper form, they will be stored in a locker on the test facility separately from this consent form; if they are stored electronically or filed for statistics and analysis, they will be stored in a password. In a dedicated computer with appropriate anti-virus software. All data and information will be preserved for at least two years. If the research and development of an experimental drug is terminated, it will be preserved for at least two years after the trial is officially stopped and destroy. If the above data and information are transferred to foreign countries for analysis and statistics, you will still be protected in compliance with the laws and regulations of your country. The project host and related teams will try their best to ensure that your personal information is properly protected.

Possible side effects, incidence and treatment methods:

1. Risks associated with the trial drug (side effects of the drug used in this trial)

All experimental drugs may cause side effects, and you may or may not experience the following side effects.

side effect:

A side effect (incidence rate <1%)

Drug leakage, treatment method: The iron leaks to the local tissues of the infusion site. After the leakage, it can cause pain, inflammation, local browning, and necrosis in severe cases. Usually no special treatment is required, and surgical treatment is necessary in severe cases.

B side effects (incidence rate <1%)

Hypotension may sometimes occur during iron infusion, which may be related to the rapid infusion and preventive use of antihistamines. It usually does not require special treatment. If the blood pressure riser is administered improperly, it may cause abnormal hemodynamics.

C side effects (incidence rate <1%)

Hydroxyl free radicals produced by intravenous iron can also damage the liver. To avoid iron

overload, iron overload is a factor that continues to aggravate liver damage. This study excluded people with abnormal liver function

D side effects (incidence rate <1%)
There is more free iron in the bloodstream during intravenous iron supplementation, which helps bacteria grow. Therefore, this study excluded people with infection.

E side effects (incidence rate <1%)

For patients with a history of multiple drug allergies, atopic allergies, and systemic inflammatory diseases such as systemic lupus erythematosus and rheumatoid arthritis, we will be extra cautious when using intravenous iron, because the chance of allergic reactions is greater. Even if the iron test is negative, it does not mean that there is no hypersensitivity reaction. Even if some iron test does not need to test, we will have to monitor it closely for at least 30 minutes every time we use iron. The light ones do not need to be dealt with, and the severe ones may be life-threatening if they are not dealt with in time. Common reactions include:
(1) Mild conditions include skin itching, flushing, fever, tight chest, urticaria, back pain, and high blood pressure.
(2) In addition to mild symptoms, moderate can also include cough, nausea, dyspnea, tachycardia, and hypotension.
(3) In severe cases, the symptoms are severe, frequent and sudden, including wheezing, periorbital edema, cyanosis, loss of consciousness, and cardiac or respiratory arrest.
F side effects (incidence rate <1%)

Increasing the iron dose will cause damage to other organs due to iron overload. The most common overload is in the liver. We will closely monitor the TSAT, and we will also closely track the liver index (GOT, GPT). If it is suspected, the iron will be stopped immediately. And arrange nuclear magnetic resonance, if necessary, further arrange liver biopsy to confirm the diagnosis.

When side effects occur: Stop the injection immediately, monitor vital signs closely, and give anti-allergic drugs if necessary.
This trial may have other side effects, but it is not yet clear. During the trial period, the trial physician and other trial personnel will regularly monitor you for side effects. If necessary, you will be arranged for additional visits and tests. If you experience side effects, please inform your trial physician and other trial personnel, and the trial physician will decide on appropriate treatment based on your situation.

Risks associated with the test process
During the trial, you may feel uncomfortable, and certain tests may be dangerous, such as: blood sample collection, electrocardiogram test, liver biopsy... etc.

Collect blood samples: Taking blood from the arm may cause pain, bruising, and dizziness, and infection may occur at a very low rate. The treatment method is to press the blood sampling site for at least 5 minutes after the blood draw; bruises can be relieved by hot compress; dizziness requires

sitting or lying down. If the blood sampling site is infected, please contact Dr. Hugo Y.-H. Lin, the host of this study immediately, and the hospital will provide you with the necessary medical care

If you experience any of the above serious or dangerous side effects, you should as soon as possible:
1. Call the 24-hour emergency contact person.
Go to the nearest emergency room as needed.
Psychological aspect-the subject may have psychological effects when participating in this trial, such as feeling pressure to receive additional treatment for dialysis due to anemia.
Social aspects-the possible impact of subjects and their relatives or ethnic groups, such as pressure to join a clinical trial.

7. Other alternative therapies and instructions:
You do not have to participate in this trial to improve your disease. If you do not participate in this trial, your disease can also be treated with the original iron riding dose, including drugs that have been approved or used to treat your disease. Your trial physician can discuss the risks and advantages of these alternative therapies with you. In addition, you can discuss your options with your routine care physician.

Expected benefits of the test:
In the past, human experience shows that when the dose of iron is increased, it can improve anemia and reduce the chance of blood transfusion.
Even with the above information, there is still no guarantee that your condition will get better by participating in this trial or will bring you other direct benefits.
What are the possible benefits of participating in this trial?
You may not benefit from participating in this trial. Tests are a way for physicians to understand whether drugs are effective in fighting disease.
The information you get from participating in this trial may help patients on hemodialysis to better understand the efficacy and safety. It may also benefit other patients with the same disease in the future.

9. The contraindications, restrictions and cooperation items of subjects during the trial:
During your participation in this trial, for your safety, please cooperate with the following matters:
-Should not participate in other clinical studies.
-Provide your past medical history, medical records and correct information related to your current condition
-For your safety, please return to the clinic at the agreed time. If you cannot come at the originally agreed time, please contact the test staff. -Please fill in the log on time and record your condition truthfully. (According to the plan book)
-For your safety, please inform the trial physician of any uncomfortable symptoms you have.
-Do not take other drugs arbitrarily, including proprietary medicines, Chinese herbal medicines,

health foods, etc. If you need to use other drugs, please discuss with your trial physician. (According to the plan book)
-If other physicians prescribe new drugs or change drugs, even for diseases unrelated to the trial, please inform the trial physician.
-If you have any questions, please do not hesitate to ask directly with your test staff (doctors, nurses).
-Don't get pregnant or let people get pregnant. If you are still likely to become pregnant or give birth to pregnancy, please use high-efficiency contraceptive methods during the trial, such as intrauterine contraceptive devices and hormonal contraceptives. (According to the plan book)
-If you seek temporary medical treatment in other medical institutions, please show to the medical staff that you are using an experimental drug.
-If you have been hospitalized or your medical condition changes between two visits, or if you wish to stop using the trial drug (or have stopped the drug), please notify your trial physician.

10. Data/sample processing method after the study:
□Agree to continue to provide Kaohsiung Medical University and affiliated institutions of Kaohsiung Medical University and other related businesses to conduct other research in a non-disconnected manner. If it exceeds the scope of my consent to use the sample, I will be referred by the original attending physician and my consent will be obtained again. Before I can use my specimen for new research, the consent form and research plan must be reviewed by the KMUIRB
□Agree to donate to Kaohsiung Medical University, Kaohsiung Medical University affiliated institutions, and related undertakings to save the human body .biological database (after unlinking, follow-up medical research can be done, and no personal privacy is involved).
□ Destroyed by Kaohsiung Medical University and its affiliates and related undertakings.
□Return (Since the remaining specimens may be lesion tissues, and their preservation and carrying may also be dangerous for infection, it is recommended that if there is no special requirement and preservation equipment, it should be destroyed by Kaohsiung Medical University and Kaohsiung Medical University affiliates and related businesses).

11. Medical ethics considerations of the experiment:
Researchers are reviewed and approved by the KMUIRB before conducting research, and follow the three major principles of medical ethics: autonomy, non-harm, and fairness. In terms of the principle of autonomy, the researcher will assess your physical and mental condition before accepting the case, and then carefully explain the research theme, purpose, and method of research to you after meeting the conditions to ensure that you receive sufficient information, and manage to think in the future. In the case of coercion or manipulation, voluntarily participate in the experiment, obtain your consent and fill out the consent form before proceeding. During the study period, you have absolute autonomy and can decide to withdraw from this study at any time, and it will absolutely not affect the medical treatment or treatment rights and the quality of care.
Regarding the principle of no harm, this research gives priority to respect for human rights and ethical considerations. Any data that can identify you will be processed in a coded manner to keep it

confidential. All data collected in the research is for academic research reference only. Disclosure with your permission. The research consent form and research results will be kept separately and kept properly to ensure that the information you provide is not leaked. In terms of the principle of fairness, the subjects of the case shall not be treated differently due to their socioeconomic status, personal characteristics, race, gender or health status. During the research, information related to your health or disease will be provided in real time, and you will be provided with consultation methods and contact telephone numbers for any research-related issues to achieve fairness.

12. Confidentiality:

Dr. Lin will treat your information as confidential in accordance with the law. During the research period, the sample/data will replace the subject's personal data with a code to protect the subject's privacy. You also understand that clinical trial monitors, auditors, competent authorities and the human trial review committee of this hospital have the right to review your research data to ensure that the clinical trial process or data meets the requirements of relevant laws and regulations, and will comply with the ethics of confidentiality.

13. Use of research results

1. The research results of this project will be published in academic journals.
2. If the research results of this project are published in academic literature, you agree to donate to Kaohsiung Medical University/Kaohsiung Medical University Hospital/Kaohsiung City Xiaogang Hospital/Kaohsiung Municipal Ta-Tung Hospital, KMU for disease diagnosis, prevention, treatment and research And other medical uses.

14. Subsidies, expenses, damages and insurance

A. Subsidies for participating in the experiment:

i There is no subsidy for this trial.

B. Financial burden:

i You do not need to bear any expenses related to this test to participate in this test. If the clinical trial plan is formulated in accordance with this research institute, the trial execution agency Datong Hospital shall be liable for compensation and compensation in accordance with the law for damage caused by adverse reactions. However, the expected adverse reactions recorded in this subject's consent form will not be compensated.

C. If adverse reactions or damage occur as a result of the clinical trial plan set by this research institute, our hospital is willing to provide professional medical care and medical consultation.

D. Except for the first two compensation and medical care, this study does not provide other forms of compensation. If you are unwilling to accept such risks, please do not participate in the trial.

E. You will not lose any legal rights by signing this consent form.

F. Liability insurance is not insured in this study.

15. Subject rights:

A. During the trial, any major findings related to your (you) health or illness that may affect your (you) willingness to continue the clinical trial will be provided to you (you) immediately.

B. In order to carry out the research work, you (you) must be under the care of Dr. Hugo Y.-H. Lin / Dr. Shengwen Niu/ Dr. I-Ching Kuo. If you (you) have any questions or conditions at present or during the trial, please feel welcome. You can contact the project host, Dr. Lin (24-hour contact number: +886-975356145).

This consent form is in duplicate. The researcher has given you (you) a copy of the consent form and has fully explained the nature and purpose of this research. Researcher Dr. Lin has answered your questions about drugs/research.

C. If you (you) have questions about the nature of the trial work during the trial, if you have opinions about your rights as a patient or suspect that you have been harmed by participating in the research, you can contact the human trial review committee of this hospital for consultation. The number is: +886-7-3121101 extension 6646 or +886-7-3133525.

This research plan has been reviewed and approved by the Institutional Review Boards (IRB) before it can be implemented. The KMUIRB is composed of professionals with a medical background and social justice persons with a non-medical background in accordance with the regulations of the Ministry of Health and Welfare, Taiwan. It is an independent committee that performs review, approval and supervision of human research cases to protect the research subjects. Rights, safety and well-being.

A. The human test review committee reviews research plans, comprehensively evaluates the appropriateness of research methods and procedures, respects the autonomy of the research subjects, ensures that the risks and interests of the research are balanced, minimizes the harm to the research subjects, and takes into account the research burden and results The fair distribution to protect the rights of research objects.

B. Any research case has risks, please evaluate carefully!

16. Withdrawal and suspension of the test:

You are free to decide whether to participate in this trial; you can also withdraw your consent at any time during the trial, and you can withdraw from the trial without any reason, and will not cause any unpleasantness or affect the medical care of your doctor in the future. Dr. Lin [the trial host or trial consignor] may also suspend the progress of the trial when necessary. When the trial is aborted or terminated, Dr. Lin [the trial host or trial consignor] will notify you immediately and ensure that you have appropriate Treatment and tracking

17. Data/sample processing method after exiting halfway:

□Agree to continue to provide Kaohsiung Medical University and affiliated institutions of Kaohsiung Medical University and related businesses to conduct other research in a non-disconnected manner. If it exceeds the scope of my consent to use the sample, I need to get my consent again before using my sample To conduct new research, the consent form and research plan must first pass the review of the KMUIRB afiiliated to Kaohsiung Medical University.

□Agree to donate to Kaohsiung Medical University, Kaohsiung Medical University affiliated institutions, and related undertakings to save the human body biological database (after unlinking, follow-up medical research can be done, and no personal privacy is involved).

□ Destroyed by Kaohsiung Medical University and its affiliates and related undertakings.
□Return (Since the remaining specimens may be lesion tissues, and their preservation and carrying may also be dangerous for infection, it is recommended that if there is no special requirement and preservation equipment, the Kaohsiung Medical University and Kaohsiung Medical University affiliates and related businesses should be destroyed).

18. Research the expected commercial benefits:
This research is not expected to derive patent rights or other commercial benefits.

19. signature

1. The trial host, or co-host or their authorized personnel have explained in detail the nature and purpose of the above-mentioned research methods in this research project, as well as the possible risks and benefit.

Signature of test host/co-host: _____ Date: _____year____month____day

Signature of other researchers participating in the interpretation and discussion during the process of obtaining consent: _____ Date: _____year____month____day

2. After the explanation, I have understood the above-mentioned research methods and the possible dangers and benefits in detail, and I have also obtained detailed explanations about the questions about this test plan. I agree to accept and voluntarily participate in this research, and will hold a copy of the consent form.

Subject’ s signature: Date: _____year____month____day

Date of birth: _____year____month____day Tel:

Uniform Number of National ID Card: Gender:

mailing address:

When the subject is an incapacitated person (a minor under the age of seven) or a person declared under guardianship, the consent of his legal representative or guardian shall be obtained.

□ When the subject is a person with restricted capacity (a minor over seven but under 20) or a person subject to an auxiliary declaration, the consent of himself and his legal agent or auxiliary shall be obtained.

□Though the subject is not incapacitated, restricted in capacity, declared under guardianship, or declared assisted, if the subject is unable to do it on his own due to unconsciousness or insanity, it shall be done by a person with the right to consent. The order of persons with the right to consent in the preceding paragraph is (1) spouse (2) adult children (3) parents (4) brothers and sisters (5) grandparents.

※Legal representative/guardian/auxiliary/person with consent

Signature: Date: Year Month Day

Relationship with the subject: Telephone number:

mailing address:

A. This is to certify that the project host has fully explained the contents of this study to the subjects.

Witness Signature: Date: Year Month Day

※1. When the subject, the legal representative/guardian/auxiliary or the person with the right of consent cannot read it, the witness should be present to participate in all discussions about the subject's consent form. Witnesses should read the subject's consent form and provide any other written information of the subject to witness that the trial host or the person designated by it has accurately conveyed its content to the subject, legal representative or person with consent Explain and make sure that they fully understand the content of all materials.

2. Subjects, legal representatives/guardians/auxiliary persons or persons with the right of consent should still sign the subject's consent form and specify the date. However, fingerprints can replace signatures.

3. After the witness completes the oral explanation and confirms that the consent of the subject, the legal representative or the person with the right to consent is entirely out of their free will, they should sign the subject's consent form and specify the date.

4. Personnel involved in the test shall not be witnesses.