Genovate Biotechnology Co., Ltd.
健亞生物科技股份有限公司

生技產業趨勢與浩宇生醫的發展狀況

9 September 2020

與新冠肺炎疫苗的距離

- 目前已有>150個候選疫苗正在開發中，其中>21個進入到臨床階段。

開發單位	疫苗種類	臨床進度
Sinopharm (國藥控股)/中國研究單位	不活化疫苗	Phase III (06/2020)
Sinovac 科興	不活化疫苗	Phase I/II
CanSino 康希諾	腺病毒載體	Phase II
牛津大學/AstraZeneca	腺病毒載體	Phase II/III
Moderna/NIH	mRNA	Phase II, phase III (07/2020)
BioNTech/Pfizer	mRNA	Phase I/II
Inovio	DNA	Phase I
Novavax	次單位疫苗	Phase I/II
Clover 三葉草	次單位疫苗	Phase I

優缺點比較

- 當大流行發生時，如何在短時間內生產足夠的疫苗量依舊是個需要克服的難題。病毒載體疫苗、核酸疫苗等技術被寄予厚望。

	病毒載體疫苗	DNA疫苗	RNA疫苗
優點	1. 接近自然感染的狀況，有機會誘導出類似的免疫反應。 2. 多抗原。	1. 最接近抗原在受感染細胞中的生成情況。 2. 適用於各種抗原。 3. 製造簡單、快速。	1. 最接近抗原在受感染細胞中的生成情況。 2. 適用於各種抗原。 3. 製造簡單、快速。 4. 相較DNA疫苗，不須有特殊施打裝置。
缺點	1. 病毒基因組可能與人體基因組發生重整。 2. 細胞培養，製程較複雜且昂貴。 3. 若已對病毒載體具免疫力，可能會減弱疫苗的效果。	1. DNA可存續的時間待釐清。 2. 送入的DNA有嵌入原有基因組之風險。	1. RNA在細胞中不穩定及不易被細胞吞入等問題需克服。
上市產品	只有動物疫苗	無	無

CAPITAL

台灣現況

開發單位	疫苗種類	進度
中研院	1. 次單元疫苗 2. 類病毒顆粒疫苗 3. 減毒牛痘病毒疫苗 4. 奈米疫苗	開發中，即將進入動物實驗。
國衛院	1. 合成胜肽疫苗 2. 重組病毒疫苗 3. DNA疫苗 4. 次單位疫苗	由初步數據評估，選定DNA疫苗為後續開發主軸，與安特羅合作。
國光	次單位疫苗	動物實驗進行中，預計08/2020開始臨床一期試驗。
高端	次單位疫苗	動物實驗進行中，，預計3Q20開始臨床一期試驗。

要快，更要安全

- 04/2016，Dengvaxia在菲律賓上市，其為全球第一個登革熱疫苗，菲律賓則為第一個核可的國家。
- 11/2017，Sanofi 限縮其使用範圍至"僅限曾感染過登革熱者"。因臨床數據顯示未感染過登革熱者施打此疫苗有可能導致更嚴重的感染症狀。此時已有超過83萬兒童接種疫苗，新聞報導，部分兒童的死亡可能與此有關。
- 02/2018，菲律賓向Sanofi提出告訴。02/2019，菲律賓衛生單位撤銷疫苗許可證。

COPCOV: Hydroxychloroquine trial to restart

30 Jun 2020

- The COPCOV trial will see chloroquine, hydroxychloroquine or a placebo given to more than 40,000 healthcare workers from Europe, Africa, Asia and South America.
- One of the lead researchers, Prof Sir Nicholas White from the University of Oxford, said: "Hydroxychloroquine could still prevent infections, and this needs to be determined in a randomised controlled trial."
- Co-investigator Prof Martin Llewelyn, from the Brighton and Sussex Medical School, said: "Although rates of coronavirus are low just now in the UK, healthcare workers are still being affected across the NHS and a second wave of infection this winter is widely expected.
- Although studies suggest hydroxychloroquine is not a life-saver for people who are already ill with coronavirus, researchers are keen to continue exploring whether it might prevent infections.
- UK regulators say hydroxychloroquine and a similar drug chloroquine can be given to healthcare workers in a clinical study to test the theory. Recruitment to the COPCOV trial had been paused amid concerns about side-effects raised by other research that has since been discredited.

Source: BBC news, 30 Jun 2020. (NCT04303507)

COVID-SHIELD FAQs

- The COVID-SHIELD is exclusively looking at hydroxychloroquine as a preventative therapy for COVID-19. The trial is not using the drug in people who have tested positive for COVID-19 or as a treatment for people who are sick with COVID-19.
- There are several examples of drugs that are effective in preventing diseases but less effective in treating them, such as antiretroviral drugs used for pre-exposure prophylaxis (PrEP) to HIV and neuraminidase inhibitor drugs (oseltamivir (Tamiflu®) and zanamivir (Relenza®)) used for influenza.
- Hydroxychloroquine has been in clinical use for decades and is currently being taken by thousands of Australians for rheumatic conditions. Like any medication, hydroxychloroquine has certain side effects, but fortunately these are well known and quite uncommon.
- There is currently no evidence from randomised, double-blinded clinical trials to suggest that hydroxychloroquine will either work or not work as a pre-exposure preventative agent in healthy people, which is why this trial is being pursued.

Source: The Walter and Eliza Hall Institute of Medical Research website. (ACTRN12620000501943)

A Multicenter, randomized, open-label, controlled trial to evaluate the efficacy and tolerability of hydroxychloroquine and a retrospective study in adult patients with mild to moderate Coronavirus disease 2019 (COVID-19)

Cheng-Pin Chen, Yi-Chun Lin, Tsung-Chia Chen, Ting-Yu Tseng, Hon-Lai Wong, Cheng-Yu Kuo, Wu-Pu Lin, Sz-Rung Huang, Wei-Yao Wang, Jia-Hung Liao, Chung-Shin Liao, Yuan-Pin Hung, Tse-Hung Lin, Tz-Yan Chang, Chin-Fu Hsiao, Yi-Wen Huang, Wei-Sheng Chung, Chien-Yu Cheng, Shu-Hsing Cheng

doi: https://doi.org/10.1101/2020.07.08.20148841

Abstract

Objective In this study, we evaluated the efficacy of hydroxychloroquine (HCQ) against coronavirus disease 2019 (COVID-19) via a randomized controlled trial (RCT) and a retrospective study. Methods Subjects admitted to 11 designated public hospitals in Taiwan between April 1 and May 31, 2020, with COVID-19 diagnosis confirmed by pharyngeal real-time RT-PCR for SARS-CoV-2, were randomized at a 2:1 ratio and stratified by mild or moderate illness. HCQ 400 mg twice for 1 d and HCQ 200 mg twice daily for 6 days were administered. Both study group and controlled group received standard of care (SOC). Pharyngeal swabs and sputum were collected every other day. The proportion and time to negative viral PCR were assessed on day 14. In the retrospective study, medical records were reviewed for patients admitted before March 31, 2020. Results There were 33 and 37 cases in the RCT and retrospective study, respectively. In the RCT, the median times to negative rRT-PCR from randomization to hospital day 14 were 5 days (95% CI; 1-9 days) and 10 days (95% CI; 2-12 days) for the HCQ and SOC groups, respectively (p = 0.40). On day 14, 81.0% (17/21) and 75.0% (9/12) of the subjects in the HCQ and SOC groups, respectively, had undetected virus (p = 0.36). In the retrospective study, 12 (42.9%) in the HCQ group and 5 (55.6%) in the control group had negative rRT-PCR results on hospital day 14 (p = 0.70). Conclusions Neither study demonstrated that HCQ shortened viral shedding in mild to moderate COVID-19 subjects.

GV17-具開發潛力的利基新藥

- 與**HCQ**比較

項目	GV17	HCQ
血中濃度穩定性	高	低
藥效	高	低
安全性	高	低
對心臟影響	低	高

- 可依需要，開發為**Lupus** 相關疾病的**505b2**新藥與**COVID-19**預防性（**PrEP**或**PEP**）藥物選項。
- 完成多項專利申請。
- 已申請美國 **FDA**的**pre-IND meeting**，規劃臨床設計與開發策略。

Gilead kicks off clinical trial of inhaled remdesivir for less-severe COVID-19

by Angus Liu | Jul 9, 2020 11:09am

- **Gilead Sciences wasted no time beginning testing of an inhaled formulation of its COVID-19 drug remdesivir.**

  - **Two weeks after securing an FDA go-ahead, the biotech on Wednesday said it had kicked off a phase 1b trial to evaluate the safety of inhaled remdesivir in 60 healthy volunteers in the U.S.**
    The hope is that the inhaled formulation—as compared with the drug's currently available intravenous form—could reach the outpatient setting, where patients have less severe disease, and that early treatment could help them avoid hospitalization.
  - **Gilead argues that delivering the antiviral directly to the lungs, where the viral infection is worst, might lead to better outcomes for early-stage COVID-19 patients who don't need to be hospitalized.**
    "Based on current scientific understanding, the upper respiratory tract is the most prevalent site of SARS-CoV-2 infection early in disease," Gilead's chief medical officer, Merdad Parsey, said in a statement.
  - **"Delivering remdesivir directly to the primary site of infection with a nebulized, inhaled solution may enable more targeted and accessible administration in non-hospitalized patients and potentially lower systemic exposure to the drug," Parsey explained.**

台微體新冠肺炎新治療方案TLC19啟動臨床試驗

增加肺部暴露量、降低劑量與心毒性以解決口服劑型侷限； 價格合理、容易取得與使用的治療/預防COVID-19方案

- 羥氯喹寧(hydroxychloroquine, HCQ)是否仍是預防及治療新冠肺炎的潛力藥物? 文獻指出，HCQ在體外模型中能夠防止細胞內胞器的酸化並抑制病毒基因的釋放，亦會促使宿主細胞上的ACE2受體醣基化，並降低該受體與COVID-19病毒表面刺狀蛋白的結合率，進而降低新冠肺炎感染及複製的機率，由細胞分子層次看來，HCQ絕對是預防及治療新冠肺炎的潛力藥物。

- TLC19在使用上需搭配醫用篩孔式霧化器投藥，故台微體與專精於研發呼吸道傳輸給藥技術的微邦科技合作，借助於微邦科技團隊在開發醫用霧化模組和產品的豐富經驗及其經ISO 17025認證霧化給藥分析實驗室檢測能量，應可加速TLC19微脂體霧化吸入劑型的開發。

- 台微體總經理葉志鴻表示：我們計畫於台灣以最快的速度完成TLC19一期臨床試驗，在健康人研究蒐集此新微脂體劑型、新吸入途徑的藥動學與安全數據，以作為後續用於COVID-19病人劑量推估的基礎。隨後規劃於美國和其他疫情嚴重的國家進行二/三期COVID-19臨床試驗。

Source：台灣微脂體(股)公司2020-08-14新聞發佈

瑞樂沙旋達碟吸入劑®Relenza®

中文藥名	英文藥名	主成分	含量	藥品外觀
瑞樂沙旋達碟吸入劑	Relenza ®	Zanamivir	5mg/劑量	

作用

治療及預防成人及兒童（>5歲）之A型及B型流行性感冒。

用法

1. 請遵照醫師處方之用法及劑量服用。
2. 治療流行性感冒：每日二次，每次二個劑量（10毫克），連續五天。
3. 預防流行性感冒：每日一次，每次二個劑量（10毫克），連續十天。

裝置說明

A. **上蓋**：掀開可將刺針刺破含藥泡殼。
B. **刺針**：刺破含藥泡殼準備上藥。
C. **指握部分（按壓）**：將滑盤從主體取出。
D. **轉盤**：置入含藥泡殼（一片四個泡殼）。
E. **吸嘴**：兩側各有一個氣孔。

Source：奇美醫療體系-衛教資訊網

Inhaled hydroxychloroquine to improve efficacy and reduce harm in the treatment of COVID-19

Med Hypotheses. 2020 Oct; 143: 110110.
Published online 2020 Jul 15

Abstract

Current formulations and dose regimens of hydroxychloroquine (HCQ) put patients at risk of harm. An analysis of clinical trials registered on ClinicalTrials.gov revealed that this may continue as many studies combine HCQ with agents that prolong the QT interval. Further, almost all of the trials registered do not consider dosage adjustment in the elderly, a patient population most likely to require HCQ treatment. Here we describe an inhaled formulation of HCQ which has passed safety studies in clinical trials for the treatment of asthma and discuss how this approach may reduce side-effects and improve efficacy. As this simple formulation progressed to phase II studies, safety data can be used to immediately enable phase II trials in COVID-19.

FDA Approves Zepzelca for Metastatic Small-Cell Lung Cancer on June 15, 2020

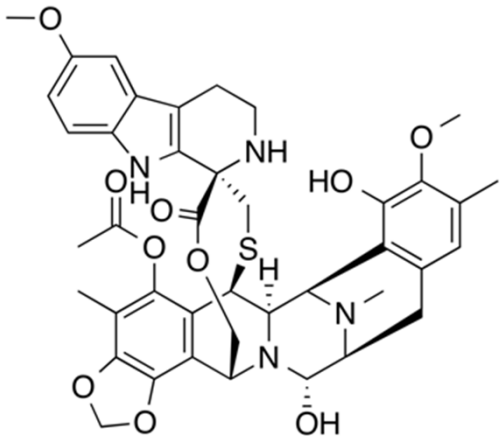
- **Lurbinectedin shrank tumors in a third of people with this less common type of lung cancer.**

  - **"Lurbinectedin is the first new drug approved for second-line treatment [of SCLC] since 1996," Charles Rudin, MD, PhD, of Memorial Sloan Kettering Cancer Center in New York City.**
  - **Zepzelca, from Jazz Pharmaceuticals and PharmaMar, is an alkylating agent that binds to DNA and interferes with transcription factors that play a role in cancer cell growth. The drug, derived from a compound isolated from sea squirts, also inhibits the activity of certain immune cells and the production of cytokines that spur tumor growth.**
  - **The FDA approval of Zepzelca is based on monotherapy clinical data from an open-label, multi-center, single-arm study in 105 adult platinum-sensitive and platinum-resistant patients with SCLC who had disease progression after treatment with platinum-based chemotherapy.[2] The data, which appeared in The Lancet Oncology May 2020 issue, showed that in patients with relapsed SCLC, Zepzelca demonstrated an ORR of 35 percent and a median duration of response of 5.3 months as measured by investigator assessment (30 percent and 5.1 months respectively, as measured by an independent review committee (IRC)). [1]**
  - **Therapies that receive accelerated approval based on overall response rates are expected to undergo further testing in larger randomized trials to confirm clinical benefits, and the FDA can rescind approval if they don't measure up.**

Source: June 16, 2020 • By Liz Highleyman

Jazz Pharmaceuticals plc June 15,2020, 5:35 ET

最惡霸癌王是它！「小細胞肺癌」終現新療法



History:

2001-08 PharmaMar filed chemical patent [GB]

(2011~2017 8 Phase I trials)

(2012~2018 3 Phase II trials)

2015/8~2016/8 Phase II, small cell lung cancer, 39 participants.

2015/5~2018/10 Phase II/III, ovarian cancer, 442 participants.

2016/8~2020/2 Phase II/III, small cell lung cancer, 613 participants.

Pivotal trial: small cell lung cancer, 105 participants.

2018-08 FDA approved orphan desgnation

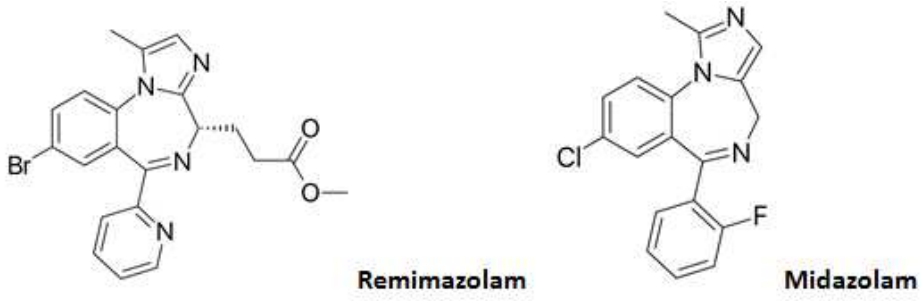
2019-09 EU approved orphan designation.

2019-12-17 NDA submitted to FDA

2020-06-15 NDA approval

Acacia Pharma Announces US FDA Approval of BYFAVO™ (remimazolam) for injection for the Induction and Maintenance of Procedural Sedation

July 02, 2020 14:02 ET | **Source:** Acacia Pharma Group plc



- **Remimazolam was originally discovered in the late 1990s at Glaxo Wellcome in their labs in Research Triangle Park, North Carolina.**
- **A Phase IIa trial comparing remimazolam to midazolam for upper endoscopy was published in December 2014, finding a similar safety profile.**
- **BYFAVO (remimazolam) for injection is a benzodiazepine indicated for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less, such as colonoscopy and bronchoscopy pyocodures.**

Source: From Wikipedia, the free encyclopedia

FDA Approves First New Drug Under International Collaboration, A Treatment Option for Patients with HER2-Positive Metastatic Breast Cancer – 1/2

For Immediate Release:April 17, 2020

- **Today, as part of Project Orbis, the U.S. Food and Drug Administration approved Tukysa (tucatinib) in combination with chemotherapy (trastuzumab and capecitabine) for the treatment of adult patients with advanced forms of HER2-positive breast cancer that can't be removed with surgery, or has spread to other parts of the body, including the brain, and who have received one or more prior treatments.**

- **The FDA collaborated with the Australian Therapeutic Goods Administration (TGA), Health Canada, Health Sciences Authority (HSA, Singapore) and Swissmedic (SMC, Switzerland) on this review. This is the first Project Orbis partnership between the FDA, HSA and Swissmedic.**

- **This approval represents an additional targeted treatment option for patients with HER2-positive breast cancer. The clinical trial supporting this approval enrolled and specifically studied patients with active brain metastases in addition to the overall population enrolled, which also demonstrated benefit in this subgroup.**

FDA Approves First New Drug Under International Collaboration, A Treatment Option for Patients with HER2-Positive Metastatic Breast Cancer – 2/2

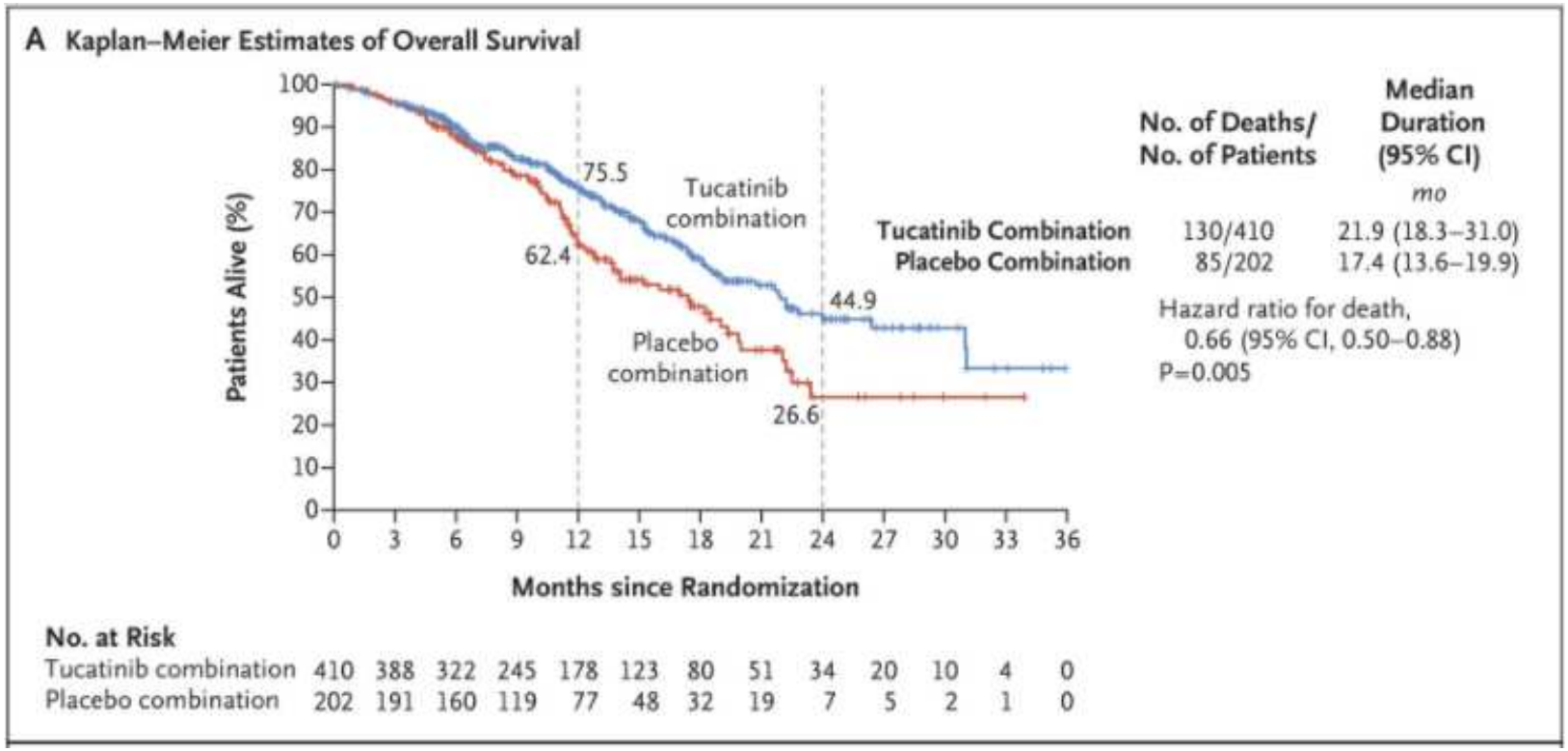
For Immediate Release:April 17, 2020

- **FDA**此次核准 **Tukysa (tucatinib)** 主要基於一項入組**612**例**HER2**突變陽性的晚期不可手術切除或轉移性乳腺癌患者的臨床試研究結果，這些患者既往接受過**Trastuzumab**、帕妥珠單株抗體和**T-DM1**治療，其中**48%**在入組時已經發生腦轉移。研究的主要終點是無進展生存期（**PFS**），次要終點是腦轉移患者的**OS**和**PFS**。

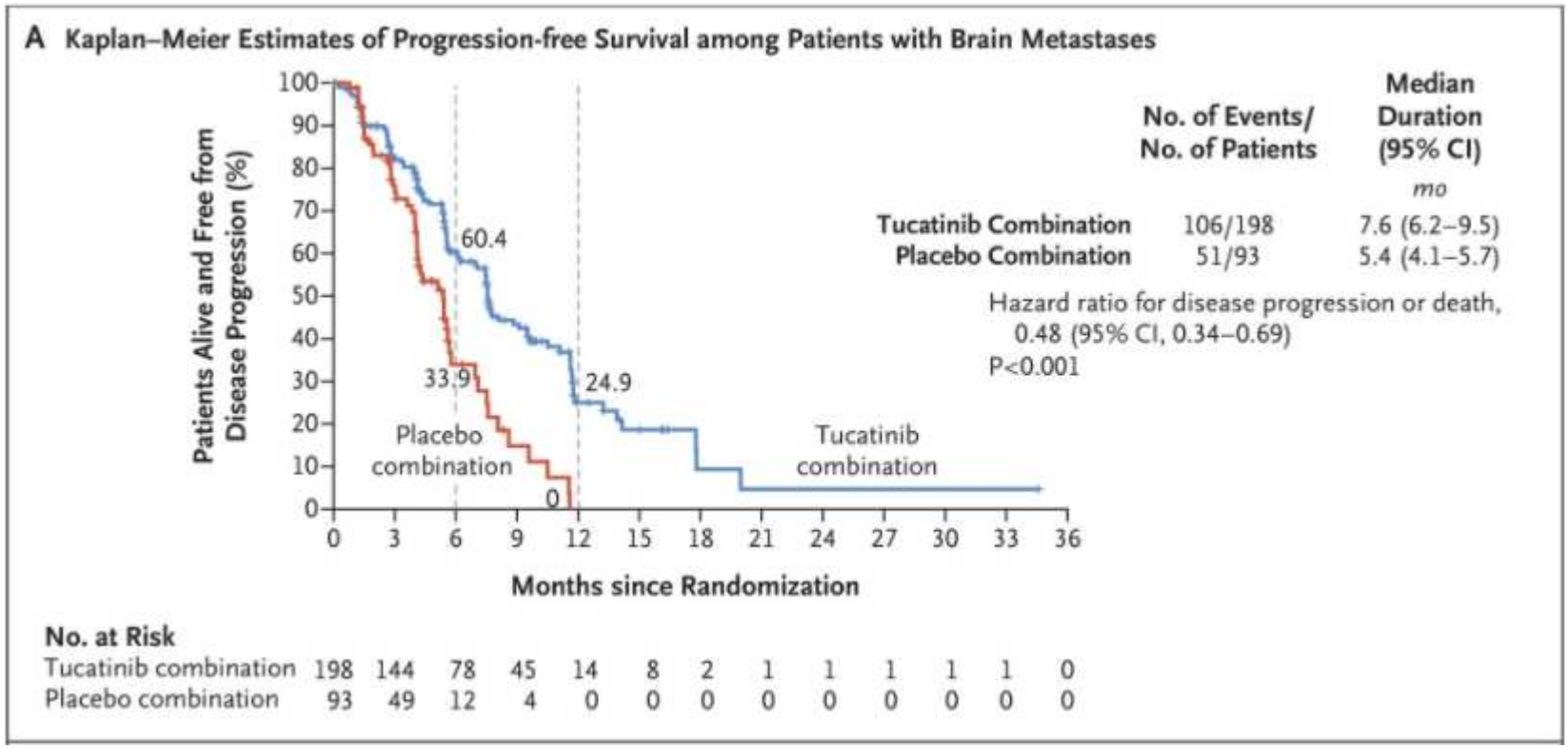
- 結果顯示，與安慰劑組**+Trastuzumab+Capecitabine**治療組相比，**Tukysa+Trastuzumab+Capecitabine**治療組患者的中位**PFS**顯著提高（**7.8 vs 5.6**個月），**OS**顯著提高（**21.9 vs 17.4**個月），腦轉移患者的**PFS**也顯著提高（**7.6 vs 5.4**個月）。

- **Tukysa was approved four months prior to the FDA goal date, providing an example of this commitment and showing how our regular work in reviewing treatments for patients with cancer is moving forward without delay.**

- **OR+PR+BTD**



Source: Murthy et al. N Engl J Med 2020; 382:597-609



Source: Murthy et al. N Engl J Med 2020; 382:597-609

FDA Approves First Drug to Image Tau Pathology in Patients Being Evaluated for Alzheimer's Disease

May 28, 2020

- **Approval Marks Significant Advance Towards a More Definitive Assessment of Alzheimer's Based on Brain Imaging**

  - **"Alzheimer's disease is a devastating condition that affects millions of Americans. This approval will provide health care professionals with a new type of brain scan to use in patients being evaluated for Alzheimer's disease," said Charles Ganley, M.D., director of Office of Specialty Medicine in FDA's Center for Drug Evaluation and Research. "While there are FDA approved imaging drugs for amyloid pathology, this is the first drug approved for imaging tau pathology, one of the two neuropathological hallmarks of Alzheimer's disease, and represents a major advance for patients with cognitive impairment being evaluated for the condition."**
  - **The first study enrolled 156 patients who were terminally ill and agreed to undergo Tauvid imaging and participate in a post-mortem brain donation program. In 64 of the patients who died within nine months of the Tauvid brain scan, evaluators' reading of the Tauvid scan was compared to post-mortem readings from independent pathologists who evaluated the density and distribution of NFTs in the same brain. The study showed evaluators reading the Tauvid images had a high probability of correctly evaluating patients with tau pathology and had an average-to-high probability of correctly evaluating patients without tau pathology.**
  - **Tauvid's ability to detect tau pathology was assessed in patients with generally severe stages of dementia and may be lower in patients in earlier stages of cognitive decline than in the patients with terminal illness who were studied.**

《BIO 2020》美國衰老研究院(NIA)主任Todd Haim：早期關鍵生物標記診斷、強化公私合作夥伴關係 突破阿茲海默症高牆

2020.06.09環球生技雜誌/記者 彭梓涵

C2N Diagnostics創新體外診斷 預測PET掃描結果

C2N Diagnostics執行長Joel Braunstein則分享該公司獨特的體外診斷、監測AD和其他神經性疾病的平台APTUS™-Aβ42/ 40，該平台是透過高靈敏度質譜進行血漿中β澱粉樣蛋白(Aβ)亞型Aβ42和Aβ40，ApoE狀態進行定量分析，可預測正子斷層造影(PET)掃描結果，該平台2019年獲得美國FDA授予突破性體外診斷，目前正在進行臨床試驗，有望近期可在CLIA認證下實驗室使用。

Joel Braunstein表示，外部良好的合作能夠促進AD產品開發，今年5月C2N Diagnostics也獲得全球獨立慈善基金會(GHR)2000萬美元計畫投資，以推進其血液檢查平台進入診所，為更多患者提供服務。

NIA資助 Cognition Therapeutics推進阿茲海默症小分子藥二期臨床

Cognition Therapeutics創辦人Susan Catalano則分享該公司目前正在推進主要候選藥物CT1812，該藥物在早期臨床研究中顯示出可減少AD症患者突觸損傷的潛力。

CT1812是一種可穿透腦部的小分子藥物，已被證明可靶向sigma-2受體，該受體是細胞損傷的反應的關鍵調節劑，CT1812可保護突觸免受有毒Aβ低聚物結合進而阻止突觸損傷和破壞。

她表示，公私合作夥伴關係對於在AD / ADRD領域推進治療至關重要，目前Cognition Therapeutics也獲得NIA大力支持，預計將授予五年內7580萬美元的贈款，以進行CT1812於540名AD患者的二期臨床試驗，這項研究也將與阿茲海默症臨床試驗聯盟(ACTC)聯合執行。

活化海馬迴，治療阿茲海默症
NaviFUS系統在澳洲獲准啟動臨床試驗-(1/2)

2020.08.17

- 今年八月七日，美國 **FDA** 受理 **Biogen**與**Eisai**合作開發的單株抗體**Aducanumab**之查驗登記，並核准其優先審查資格（**Priority Review**）。此藥物原本經過兩個三期臨床試驗之期中數據分析，顯示無法達到主要療效指標而中止試驗，然而，在重新分析臨床數據後，其中一臨床試驗顯示接受高劑量 **Aducanumab**的病人較接受安慰劑的對照組病人，在主要療效指標上達統計意義，可減緩病程進展。此單株抗體之作用機制主要在清除β類澱粉蛋白質堆積，但未標靶**Tau**蛋白且無促進神經新生作用。基於以上分析結果，美國**FDA**仍給予優先審查資格，足見在此一未被滿足的醫療需求上，美國**FDA**對於新藥物或技術冀與的高度期望。

- **NaviFUS**系統提供一嶄新的治療方式，藉由釋放聚焦式超音波能量，最深至腦內約**10**公分處，輔以精準導航作用至海馬迴，可有效且暫時地打開該部位的血腦屏障，除增加血管通透性、減少β類澱粉蛋白質與**Tau**蛋白堆積外，更可活化微膠細胞的清道夫作用並促進神經新生，以改善阿茲海默症病症的功效。前述作用已在老鼠實驗上獲得驗證，期能在澳洲的臨床試驗進一步驗證其在人體的安全性與療效。

活化海馬迴，治療阿茲海默症
NaviFUS系統在澳洲獲准啟動臨床試驗-(2/2)

2020.08.17

- **NaviFUS**在澳洲的試驗將是世界第一個用光學導引超音波裝置作用於阿茲海默病人海馬迴的臨床試驗，除了使用阿茲海默症相關量表、**β**類澱粉蛋白質與**Tau**蛋白的生物標記作為療效指標以外，我們也將以較容易觀察且阿茲海默症病人普遍出現的憂鬱症狀之改善作為探索性療效指標，檢視其作用關連性。

- 目前唯一被歐盟核准用於治療阿茲海默症且已在歐洲上市的醫療儀器為由瑞士**Storz Medical**公司（該公司隸屬於年銷售額**20**億歐元的德國知名內視鏡與和手術器械專業公司）研發的穿顱脈衝刺激（**Transcranial Pulse Stimulation, TPS**）裝置，可維持或改善部分阿茲海默症的症狀，此技術採連續重複施打單次脈衝超音波的方式，最深能刺激至腦部約**8**公分處深，但無作用於血腦屏障（**Blood Brain Barrier, BBB**）之開啟。

公司沿革

Vision: Development of novel therapy for unmet need of CNS related disorders thru non-invasive BBB opening/neuromodulation by Focused Ultrasound

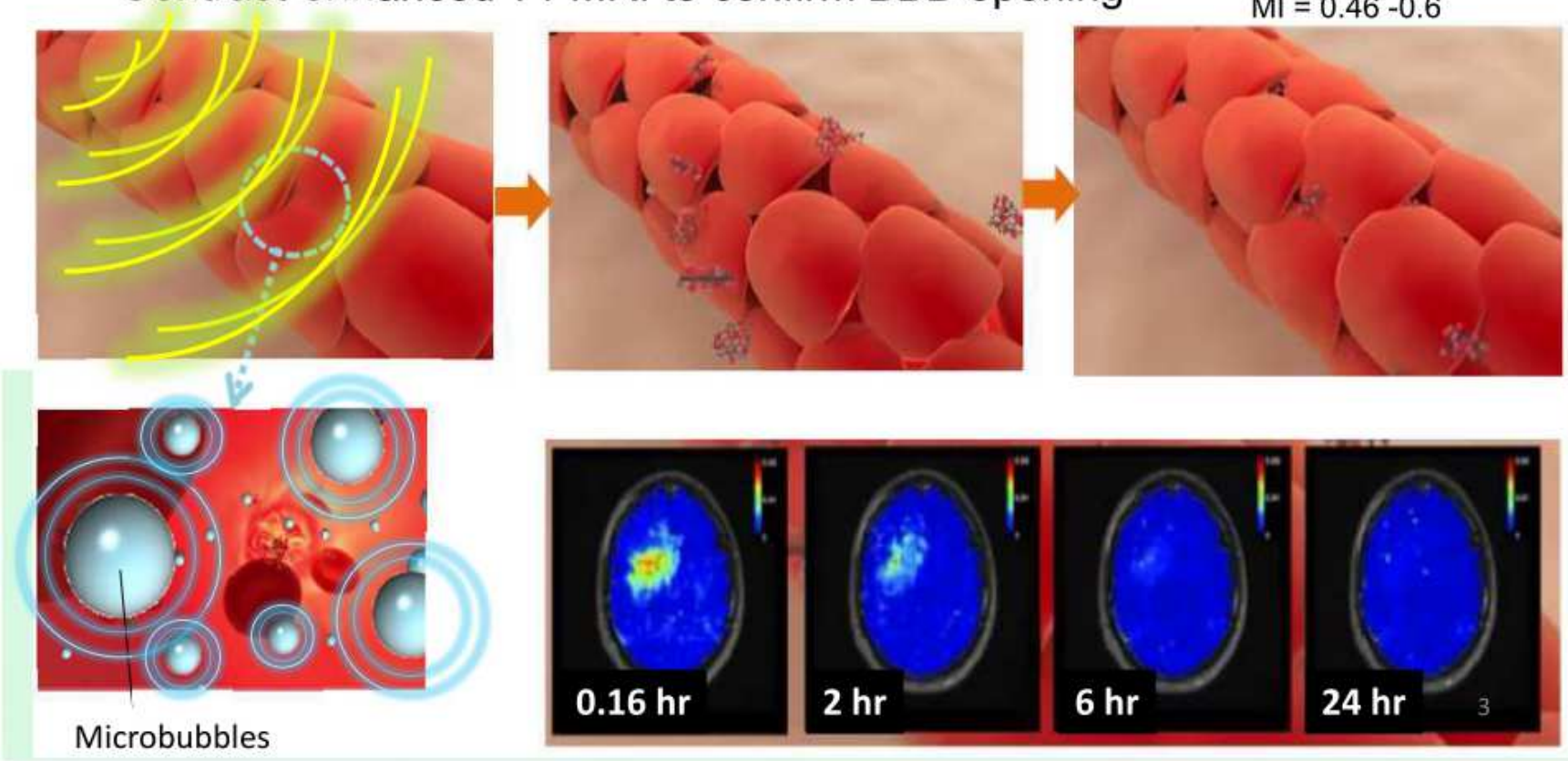
願景: 針對有迫切性需求的中樞神經異常之相關疾病，應用精準導航之穿顱聚焦超音波，以非侵入，創新的手術方式，藉由打開血腦屏障或調控神經來治療腦的疾病

- **Established in Mar, 2015**
- **Office: Taipei, Taiwan**
- **Technology transferred from Chang Gung University/ Hospital**
- **Authorized from B&W Hospital/ Harvard U /USA**
- **Capital: 4.09億 NTD, PMV : 6.1億 NTD**
- **23+2 employees**
  - 6 Ph.D.
  - 14 Master
  - 3 Bachelor

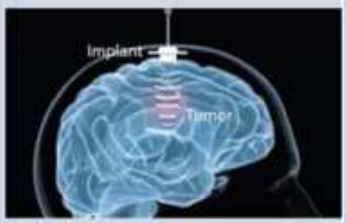
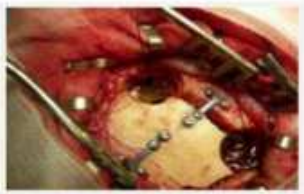
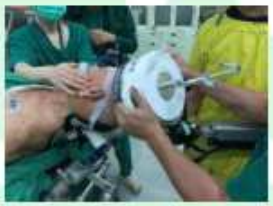
How to use Focused Ultrasound to open the Blood Brain Barrier?

- Pulsed low-pressure FUS exposure with microbubbles IV injection to induce it (Radiology, 2001; Neuroimage, 2005)
- BBB temporally opened 0.5 – 4 hrs
- Contrast-enhanced T1 MRI to confirm BBB opening

I_{spta} = 0.1-0.2 W/cm²
MI = 0.46 -0.6



Competitors & Product Stage

	SonoCloud	Exablate 4000 type-2	NaviFUS-001
Solution			
Stage	CE Phase I/II	USA Phase I/II	**TW Phase I/II**
Company	Carthera Inc.	InSightec Inc.	**NaviFUS Corp.**
Product Concept	Planar, implanted ultrasound device	Focused, transcranial ultrasound device	**Focused, transcranial Ultrasound device**
Drugs	Carboplatin	Temozolomide	**Avastin**
Guidance	During implant surgery	MRI guided	**Neuronavigation**
			

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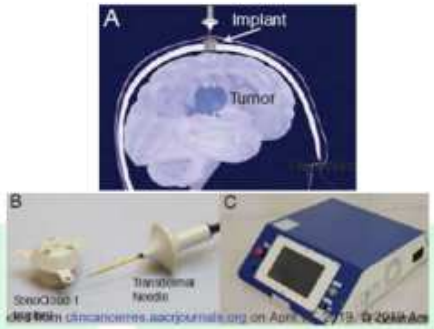
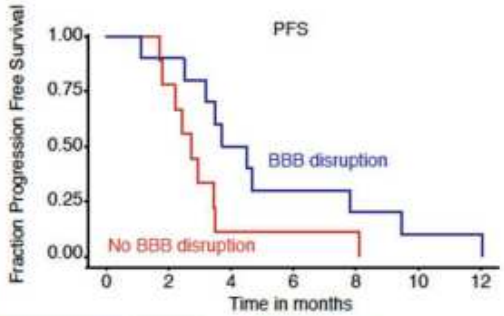
Successful Clinical Trial:
Cartherra: rGBM trial (NCT02253212)

- Interventions: **SonoCloud-1 + carboplatin**
- SonoCloud-1 treatments were well tolerated and may increase the effectiveness of systemic drug therapies, such as carboplatin, in the brain without inducing neurotoxicity.
- Median progression-free survival (mPFS): 2.73 months → 4.11 months
- Median overall survival(mOS): 8.64 months → 12.94 months





Clinical Cancer Research (2019)
DOI: 10.1158/1078-0432.CCR-18-3643

NaviFUS Clinical Trial I-a： BBB opening/ rGBM/TW

- **Milestones:**
  - rGBM, Avastin+FUS, CGMH, Taiwan
  - Increased Frequency, Drug and Tissue Volume
  - 8 pts
  - IRB approval on 12/12/2019
  - TFDA IDE approved on 03/30/2020
  - IRB contract to be done in 05/2020
  - 1st patient on 08/04/2020
  - Sponsored by FUS foundation

Clinical Trial I-b： BBB Opening/rGBM/USA (Visited Stanford in Aug 2019)

- Planning:
  - Study Titles:
    - Avastin+FUS
  - Investigator-initiated IDE in Stanford
  - 8 rGBM pts
  - IDE consultant: Greenleaf, USA
  - 04/15/2020 IDE pre-submission to FDA
  - 07/28/2020 T-conf w/ FDA w/ positive response
  - Q4 IDE submission

Clinical Trial II：Neuromodulation/Epilepsy

- Pre-clinical data submitted for publication
- Milestones
  - 2018.11.15 VGH IRB approval
  - **2019.02 TFDA approval**
  - 2019.05 SIV
  - **The 2nd Pt recruited on 2020/01/02**
  - **2020.03.11 DSMB approved!**
  - **2020.07 5th pt recruited**

NaviFUS治療後出現類似已上市產品「腦深層電刺激(DBS)」治療效應

Good Pre-clinical Outcomes *Brain Stimulation, 2019*